



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification <sup>7</sup> : A61B 17/22, A61M 37/00</p>	<p>A1</p>	<p>(11) International Publication Number: <b>WO 00/00095</b> (43) International Publication Date: 6 January 2000 (06.01.00)</p>
<p>(21) International Application Number: PCT/US99/14757 (22) International Filing Date: 29 June 1999 (29.06.99) (30) Priority Data: 09/107,078 29 June 1998 (29.06.98) US (71) Applicant: EKOS CORPORATION [US/US]; Suite 101, 22030 20th Avenue S.E., Bothell, WA 98021 (US). (72) Inventors: SHANG, John; 2123 Timber Trail, Bothell, WA 98012 (US). LICHTTENEGGER, Gary; 20927 N.E. 169th Street, Woodinville, WA 98072 (US). RODRIGUEY, James, E.; 1811 N.E. 185th Street, Seattle, WA 98155 (US). TACHIBANA, Katsuro; 6-18, Kusagae 1-chome, Chuo-ku, Fukuoka-shi, Fukuoka 810 (JP). (74) Agent: DAVIS, Paul; Wilson Sonsini Goodrich &amp; Rosati, 650 Page Mill Road, Palo Alto, CA 94304-1050 (US).</p>		<p>(81) Designated States: JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
<p>(54) Title: SHEATH FOR USE WITH AN ULTRASOUND ELEMENT</p> <p>(57) Abstract</p> <p>A system for delivering ultrasound energy to a treatment section in a vessel is disclosed. The system includes a sheath with a utility lumen and an energy delivery section at least partially constructed from a material which transmits ultrasound energy. The system also includes a drug delivery member having a plurality of drug delivery ports which are positioned adjacent the energy delivery section. The system further includes an elongated body including at least one ultrasound element and configured to be movably positioned within the utility lumen to transmit the ultrasound energy from the ultrasound element through the energy delivery section.</p>		

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**SHEATH FOR USE WITH AN ULTRASOUND ELEMENT****BACKGROUND OF THE INVENTION**5      **Field of the Invention**

The present invention relates to an ultrasound enhanced drug delivery apparatus, and more particularly, to an ultrasound element which can be movably positioned within a drug delivery sheath.

10      **Description of Related Art**

Thrombus formation is a protective and healing mechanism, however, formation of thrombi can be detrimental. For instance, if a blood vessel becomes blocked, distal tissue may be deprived of oxygen with resulting damage or necrosis. In the case of cerebral circulation, an arterial thrombus blockage is one cause of cerebral strokes. In the case of coronary thrombosis, blockage and subsequent distal tissue necrosis of cardiac muscle tissue will impair cardiac pump output, may cause electrical abnormalities, and potentially catastrophic heart failure and death. The thrombus can form at the site of artery narrowing due to arterial wall damage or disease, or the thrombus may have broken free from some proximal site only to become wedged in a distal stenosis. Thrombus can also form subsequent to attempts to remove a stenosis using balloon angioplasty or rotary atherectomy.

Ultrasound sheaths have been described specifically for removal or dissolution of thrombus (U.S. Patents: Tachibana 5,197,946; Bernstein 25 5,163,421; Weng 5,269,297). The sheaths of Bernstein and Weng place an ultrasound generator external to the body and transmit acoustic energy through a metal wire wave-guide to the distal sheath. The sheath of Tachibana includes a small ultrasound element positioned at the distal end of the sheath that is energized by electrical wires. In either case, ultrasound energy is delivered to and radiated from the distal tip of the sheath in the vicinity of a blocking thrombus. The application of ultrasound can directly emulsify nearby

thrombus through the motion of the sheath tip, associated cavitation, and bioeffects.

5 The application of ultrasound can also enhance delivery of drug into a vessel wall. There are instances where the vessel wall is diseased or has been injured during balloon angioplasty or rotary atherectomy. Narrowing of the vessel can occur in response to these injuries. Certain drugs, such as heparin, may inhibit this narrowing of the blood vessel if the drug can be delivered into the blood vessel wall. A sheath can be used to deliver drugs into any portion of the body or target organ. Ultrasound energy in the presence of these drugs  
10 can enhance the delivery through and across bodily fluids and tissue. Hence, an ultrasound drug delivery sheath placed in a blood vessel will assist delivery across the blood vessel wall, whether it be an artery or a vein, into the surrounding muscle or tissue.

The intensity of the ultrasound delivered from a cylindrical ultrasound  
15 element decreases exponentially with radial distance from the sheath tip. Hence, treatment of thrombi is limited to the circumferential area surrounding of the sheath tip of a sheath with an ultrasound element. This limited treatment area may be effective for small length clots, however, larger clots must be treated one section at a time.

20 Some thrombi can be large. For instance, a deep vein thrombus in a patient's lower leg and can have a length from several centimeters to as much as 30-50 cm long. Early treatment protocols for these long thrombi used a drug infusion sheath to drip lytic drug at one end of a thrombus. As the thrombus was dissolved, the sheath would be advanced. This process was  
25 repeated until the entire clot was dissolved. More current therapy for a deep vein thrombosis is to use an infusion sheath with drug infusion ports distributed along the lateral dimension of the sheath. The sheath can be pushed through the entire length of the clot. The thrombolytic drug is then infused throughout the lesion for a period of hours.

30 There is a need for an ultrasound sheath that is useful for treating a deep vein thrombus to enhance and accelerate the action of the thrombolytic

drug. There is a further need for an ultrasound sheath that is useful for treating vessel lesions, particularly those that have extensive lengths.

### SUMMARY OF THE INVENTION

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A system for delivering ultrasound energy to a treatment section in a vessel is disclosed. The system includes a sheath with a utility lumen and an energy delivery section at least partially constructed from a material which transmits ultrasound energy. The system also includes a drug delivery member having a plurality of drug delivery ports which are positioned adjacent the energy delivery section. The system further includes an elongated body including at least one ultrasound element and configured to be movably positioned within the utility lumen to transmit the ultrasound energy from the ultrasound element through the energy delivery section.

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In another embodiment the system includes a sheath having a utility lumen configured to movably receive an elongated body with an ultrasound element and an energy delivery section at least partially constructed from a material which transmits ultrasound energy from the ultrasound element. The system also includes a drug delivery member having a plurality of drug delivery ports which are configured to be positioned adjacent the energy delivery section.

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A sheath for delivering ultrasound energy to a treatment section in a vessel is also disclosed. The sheath includes a utility lumen configured to movably receive an elongated body with an ultrasound element. The sheath also includes an energy delivery section at least partially constructed from a material which transmits ultrasound energy from the ultrasound element. A plurality of drug delivery ports are positioned adjacent the energy delivery section.

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In another embodiment, the sheath includes a utility lumen configured to movably receive an elongated body with an ultrasound element. The sheath also includes an energy delivery section at least partially constructed from a

material which transmits ultrasound energy from the ultrasound element. At least one temperature sensor is positioned adjacent the energy delivery section.

A system for delivering ultrasound energy to a treatment section in a vessel is disclosed. The system includes a sheath having a utility lumen and an energy delivery section which is at least partially constructed from a material which transmits ultrasound energy. An expandable balloon positioned at least partially adjacent the energy delivery section. The system also includes an elongated body with at least one ultrasound element. The elongated body is configured to be movably positioned within the utility lumen to transmit the ultrasound energy from the ultrasound element through the energy delivery section.

#### BRIEF DESCRIPTION OF THE FIGURES

Figure 1A is a sideview of a sheath and elongated body according to the present invention.

Figure 1B is a sideview of a sheath and elongated body according to the present invention.

Figure 2A is a cross section of a sheath with an elongated body positioned within a utility lumen.

Figure 2B is a cross section of a sheath proximal end.

Figure 2C is a cross section of an elongated body including a body lumen.

Figure 2D is a cross section of an elongated body including a body lumen positioned within a sheath including a closed occlusion device.

Figure 2E is a cross section of an elongated body including a body lumen positioned within a sheath including a closed occlusion device.

Figure 3A is a sideview of a sheath distal end.

Figure 3B is a cross sectional view of a sheath distal end.

Figure 3C is a sideview of a sheath distal end.

Figure 3D is a cross sectional view of a sheath distal end.

Figure 3E illustrates a drug delivery member with slit shaped drug delivery ports.

Figure 3F illustrates a drug delivery member with arc shaped slits as drug delivery ports.

5        Figure 4A is a sideview of a sheath distal end with drug delivery ports of increasing size.

Figure 4B is a cross sectional view of a sheath distal end.

Figure 5 is a cross section of a sheath distal end with an integral occlusion device.

10       Figure 6A is a sideview of a sheath including a balloon.

Figure 6B is a cross section a balloon positioned at a distal end of a sheath which includes drug delivery ports configured to produce an even flow along the length of the energy delivery section.

15       Figure 6C is a cross section of a balloon positioned at a distal end of a sheath which includes an expansion lumen for expanding the balloon and delivering a drug solution.

20       Figure 6D is a cross section of a balloon positioned at a distal end of a sheath which includes an expansion lumen for expanding the balloon and drug delivery ports configured to produce an even flow along the length of the energy delivery section.

Figure 7A illustrates ultrasound elements connected in parallel.

Figure 7B illustrates ultrasound elements connected in series.

Figure 7C illustrates ultrasound elements connected with a common wire.

25       Figure 8 illustrates temperature sensors connected with a common wire.

Figure 9 is a block diagram of a feedback control system.

Figure 10A is a cross section of a treatment site.

30       Figure 10B is a sideview of a sheath distal end positioned at a treatment site.

Figure 10C is a sideview of a sheath distal end positioned at a treatment site.

Figure 10D is a sideview of a sheath proximal end.

Figure 10E is a cross section of a sheath distal end positioned at a treatment site.

5 Figure 10F illustrates an ultrasound element positioned within a utility lumen.

Figure 10G is a sideview of a sheath distal end positioned at a treatment site.

Figure 11A illustrates a balloon positioned adjacent a clot.

10 Figure 11B illustrates a balloon expanded into contact with the clot of Figure 11A.

#### DETAILED DESCRIPTION

15 The invention relates to a system for delivering ultrasound energy to a treatment section in a vessel. The system includes a sheath with an energy delivery section at least partially constructed from a material which transmits ultrasound energy. The sheath is designed to be positioned within a vessel such that at least a portion of the energy delivery section is positioned adjacent a treatment site within the vessel. The system also includes an elongated body with an ultrasound element positioned at its distal end. The elongated body  
20 can be received in a utility lumen included in the sheath such that the ultrasound element is positioned within the energy delivery section.

Ultrasound energy can be delivered from the ultrasound element through the energy delivery section to the treatment site.

25 The elongated body can be moved within the utility lumen so the ultrasound element can be moved relative to the energy delivery section. As a result, the ultrasound element can be moved within the treatment site to deliver ultrasound energy to different sections of the treatment site. The motion of the ultrasound element relative to the treatment site can help emulsify a clot,  
30 thrombus or other blockage at the treatment site. Since, the ultrasound element is being moved relative to the treatment site within the sheath, the

movement of the ultrasound element relative to the treatment site does not damage the vessel including the treatment site.

5 The elongated body can include a cooling fluid lumen which passes adjacent the ultrasound element. Similarly, a cooling fluid lumen can be formed between the elongated body and the sheath. A cooling fluid can be passed through the cooling fluid lumen to cool the ultrasound element. The heating of the ultrasound element can limit the amount of power which can be provided to the ultrasound element. Cooling the ultrasound element during its operation allows the power provided to the ultrasound element to be increased. 10 As a result, cooling the ultrasound element can increase the efficiency of the treatment. Movement of the ultrasound element can be accomplished manually or through use of an automated method.

The system can also include a drug delivery member which includes a plurality of drug delivery ports which are positioned adjacent to the energy 15 delivery section. The drug delivery ports permit delivery of a drug solution to the treatment site. Ultrasound energy can also be delivered to the treatment site to enhance the effect of the drug within the treatment site.

The drug delivery member can be external to the energy delivery section. As a result, a drug solution does not need to be delivered through the 20 energy delivery section allowing the energy delivery section to be constructed of acoustically transparent materials which cannot be easily extruded. The energy delivery section can also be very thin since a drug delivery lumen need not pass through materials comprising the energy delivery section. Thinner materials increase the acoustic transparency of the energy delivery section. 25 Suitable materials for the energy delivery section include, but are not limited to, polyimides. The portion of the sheath which is not included in the energy delivery section can be constructed from materials such as polyurethanes, copolyesters, or thermoplastic elastomers which provides the sheath with kink resistance, rigidity and structural support necessary to transport the energy 30 delivery section to the treatment site.

The sheath can also include at least one temperature sensor positioned adjacent the energy delivery section. The temperature sensors can be coupled

with a feedback control system. The feedback control system can be used to adjust the level of power delivered to the ultrasound element in response to the signal from at least one temperature sensor. As a result, the temperature at the treatment site can be maintained within a desired range during the treatment.

5           Figure 1A illustrates a drug delivery system 10 according to the present invention. The system 10 includes a sheath 12 with a sheath proximal end 14 and a sheath distal end 16. The sheath distal end 16 includes, a support section 17, an energy delivery section 18, temperature sensors 20 and an occlusion device 22. The sheath proximal end 14 includes temperature sensor leads 24 and a cooling fluid fitting 26. A utility lumen 28 extends through the sheath 12 along the length of the sheath 12. A drug delivery member 30 is positioned adjacent the energy delivery section. The drug delivery member 30 includes a drug inlet port 32 which can be coupled with a drug source via a connector such as a Luer type fitting. The drug delivery member 30 can be incorporated into the support section 17 as illustrated in Figure 1A or can external to the support section as illustrated in Figure 1B. The system 10 also includes an elongated body 34 with a body proximal end 36 and a body distal end 38. An ultrasound element 40 is positioned at the body distal end 38.

15           The elongated body 34 has an outer diameter which permits the elongated body 34 to be inserted into the utility lumen 28. Figure 2A illustrates the elongated body 34 threaded through the utility lumen 28 until the ultrasound element 40 is positioned within the energy delivery section 18. Suitable outer diameters of the elongated body 34 include, but are not limited to, .010" - .100". Suitable diameters of the utility lumen 28 include, but are not limited to .015" - .110". The utility lumen 28 extends through the occlusion device 22. The portion of the utility lumen 28 extending through the occlusion device 22 has a diameter which can accommodate a guidewire (not shown) but which prevents the ultrasound element 40 from passing through the occlusion device 22. Suitable inner diameters for the occlusion device 22 include, but are not limited to .005" - .050".

20           The ultrasound element 40 can be rotated or moved within the energy delivery section 18 as illustrated by the arrows 52 illustrated in Figure 2A.

The movement of the ultrasound element 40 within the energy delivery section 18 can be caused by manipulating the body proximal section while holding the sheath proximal section stationary. The elongated body 34 can be at least partially constructed from a material which provides enough structural support to permit movement of the elongated body 34 within the sheath 12 without kinking of the elongated body 34. Suitable materials for the elongated body 34 include, but are not limited to polyesters, polyurethanes, thermoplastic, elastomers.

As illustrated in Figure 2A, the outer diameter of the elongated body 34 can be smaller than the diameter of the utility lumen 28 to create a cooling fluid lumen 44 between the elongated body 34 and the utility lumen 28. A cooling fluid can be flowed through the cooling fluid lumen 44, past the ultrasound element 40 and through the occlusion device 22. The flowrate of the cooling fluid and/or the power to the ultrasound element 40 can be adjusted to maintain the temperature of the ultrasound element 40 within a desired range.

The sheath proximal end 14 can include a cap 46 as illustrated in Figure 2B. A cooling fluid can be flowed from the cooling fluid fitting 26 through the cooling fluid lumen 44 as illustrated by the arrows 48. The cap 46 includes a hemostasis valve 50 with an inner diameter which substantially matches the diameter of the elongated body 34. The matched diameters reduces leaking of the cooling fluid between the cap 46 and the elongated body 34.

As illustrated in Figure 2C, the ultrasound element 40 can be a hollow cylinder and the elongated body can include a body lumen 51 which extends through the ultrasound element 40. The cooling fluid can be flowed through the body lumen past the ultrasound element 40 to provide cooling to the ultrasound element 40.

As illustrated in Figure 2D, the occlusion device 22 can be integral with the sheath 12 and can have a closed end. The body lumen 51 can serve as a return lumen for the cooling fluid. As a result, the inside and the outside of the ultrasound element 40 are exposed to the cooling fluid to accelerate the

cooling of the ultrasound element 40. As illustrated in Figure 2D, the flow of the cooling fluid can be reversed so the cooling lumen serves as the return cooling fluid lumen. The above cooling schemes permit the power provided to the ultrasound element to be increased in proportion to the cooling flow rate.

5 Further, certain schemes can prevent exposure of the body to cooling fluids.

The drug delivery member 30 includes a drug delivery portion which is positioned adjacent the energy delivery section 18 as illustrated in Figure 3A. As illustrated in Figure 3B, the drug delivery member 30 includes a drug delivery lumen 56 extending through the length of the drug delivery member 30. The drug delivery member 30 also includes a series of drug delivery ports 58 coupled with the drug delivery lumen 56. A drug source coupled with the drug inlet port 32 can provide a pressure which drives a drug solution through the drug delivery lumen 56 and out the drug delivery ports 58. A suitable material for the drug delivery member 30 includes, but is not limited to,

10 15 polyimide, polyolefin, polyester.

The sheath 12 can include a plurality of drug delivery members 30. The drug delivery members 30 can be wound around the energy delivery section 18 or they can be positioned along the length of the energy delivery section 18 as illustrated in Figure 3C. Each drug delivery member 30 can be coupled with the same drug inlet port 32. In another embodiment, each drug delivery member 30 is coupled with independent drug inlet ports 32 so different drug solutions can be delivered to different drug delivery ports 58.

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The drug delivery ports 58 are positioned close enough to achieve a substantially even flow of drug solution around the circumference of the energy delivery section 18 and along the length of the energy delivery sections 18. The proximity of adjacent drug delivery ports 58 can be changed by changing the density of drug delivery ports 58 along the drug delivery member, by changing the number of windings of the drug delivery member around the energy delivery section 18 or by changing the number of drug delivery members 30 included adjacent the energy delivery section 18. A suitable displacements between adjacent drug delivery ports 58 include, but are not limited to, from 0.1" to 1.0", preferable 0.2" to 0.6".

25 30

The size of the drug delivery ports 58 can be the same or change along the length of the drug delivery member. For instance, the size of the drug delivery ports 58 distally positioned on the drug delivery section can be larger than the size of the drug delivery ports 58 which are proximally positioned on the drug delivery section. The increase in sizes of the drug delivery ports 58 can be designed to produce similar flowrates of drug solution through each drug delivery port 58. This similar flowrate increases the uniformity of drug solution flowrate along the length of the sheath 12. When the drug delivery ports 58 have similar sizes along the length of the drug delivery member, a suitable size for a drug delivery port 58 includes, but is not limited to .0005" to .0050". When the size of the drug delivery ports 58 changes along the length of the drug delivery member, suitable sizes for proximally positioned drug delivery ports 58 includes, but is not limited to from .0001" to .005" and suitable sizes for distally positioned drug delivery ports 58 includes, but is not limited to 0.0005" to 0.0020". The increase in size between adjacent drug delivery ports can be substantially uniform between or along the drug delivery member. The dimensional increase of the drug delivery ports is dependent upon material and diameter of the drug delivery member. The drug delivery ports 58 can be burnt into the drug delivery member 30 with a laser.

Uniformity of the drug solution flow along the length of the sheath 12 can also be increased by increasing the density of the drug delivery ports 58 toward the distal end of the drug delivery member.

The drug delivery ports 58 can be slits with a straight shape as illustrated in Figure 3E or an arcuate shape as illustrated in Figure 3F. The drug delivery member 30 can be constructed from materials such as polyimide, nylon, pebax, polyurethane or silicon. When the drug delivery lumen 56 is filled with drug solution, the slits remain closed until the pressure within the drug delivery lumen exceeds a threshold pressure. As the pressure within the drug delivery lumen builds, the pressure on each of the slits will be approximately uniform. Once, the threshold pressure is reached, the uniform pressure will result in the slits opening almost simultaneously and cause a nearly uniform flow of drug solution out of all the slits. When the pressure

within the drug delivery lumen 56 falls below the threshold pressure, the slits close and prevent delivery of additional drug solution. The stiffer the material used to construct the drug deliver member, the higher the threshold pressure required to open the slit shaped drug delivery ports. The slit shape can also prevent the drug delivery ports 58 from opening when exposed to low pressures from outside the sheath 12. As a result, slit shaped drug delivery ports can maximize control of drug delivery.

The sheath 12 and energy delivery section 18 can be constructed from a single material as illustrated in Figure 4A. Suitable materials include, but are not limited to polyimide, polyolefin, polyester. The entire sheath or only the sheath proximal end may be reinforced by braiding, mesh or other constructions to increase flexibility, kink resistance, and pushability. As illustrated in Figure 4A, the drug delivery ports 58 can be included in the sheath 12. The drug delivery ports 58 can be coupled with independent drug delivery lumens 28 as illustrated in Figure 4B.

The sheath can include a support section 17 which is constructed from a different material than the energy delivery section as illustrated in Figure 5. Figure 5 also illustrates the occlusion device 22 as being integral with the energy delivery section 18. The energy delivery section 18 can be constructed from a material which readily transmits ultrasound energy. The support section can be constructed from a material which provides structural strength and kink resistance. Further, the support section or the proximal end of the support section may be reinforced by braiding, mesh or other constructions to increase flexibility, kink resistance, and pushability. Suitable materials for the support section include, but are not limited to, polyimides, polyolefin, polyester. A suitable outer diameter for the support section includes, but is not limited to .020" to .200". Suitable materials for the energy delivery section 18 include, but are not limited to, polyolefins, polyimides, polyester and other low ultrasound impedance materials. Low ultrasound impedance materials are materials which readily transmit ultrasound energy with minimal absorption of the ultrasound energy.

The sheath distal end 16 can include a balloon 59 as illustrated in Figure 6A. The balloon 59 can be constructed from permeable membrane or a selectively permeable membrane which allows certain media to flow through the membrane while preventing other media from flowing through the  
5 • membrane. Suitable materials for the balloon 59 include, but are not limited to cellulose, cellulose acetate, polyvinylchloride, polyolefin, polyurethane and polysulfone. When the balloon is constructed from a permeable membrane or a selectively permeable membrane, the membrane pore sizes are preferably 5 A-2  $\mu\text{m}$ , more preferably 50 A-900 A and most preferably 100 A- 300 A in  
10 diameter.

As illustrated in Figures 6B, the balloon 59 can be positioned adjacent drug delivery ports 58. The drug delivery ports 58 can be designed so a uniform flow occurs along the length of the energy delivery section 18. This design can serve to prevent a pressure gradient from developing along the  
15 length of the balloon. Delivering a drug solution through the drug delivery ports 58 can serve to expand the balloon 59. When the balloon 59 is constructed from a membrane or a selectively permeable membrane, the drug solution can be delivered with enough pressure to drive the drug across the membrane. Various phoretic processes and apparatuses can also be used to  
20 drive the drug solution across the membrane. When the balloon 59 is constructed from a selectively permeable membrane, the pressure and/or phoresis may drive only certain components of the drug solution across the membrane while preventing other components from crossing the membrane.

The balloon 59 can also be positioned adjacent one or more expansion  
25 ports 60A coupled with an expansion lumen 60B as illustrated in Figure 6C. The drug solution can be delivered to the balloon 59 via the expansion lumen 60B. Delivering a drug solution through the expansion lumen 60B can serve to expand the balloon 59. When the balloon 59 is constructed from a  
30 membrane or a selectively permeable membrane, the drug can be delivered with enough pressure to drive the drug solution or certain components of the drug solution across the membrane. Similarly, phoretic means can also be

used to drive the drug solution or certain components of the drug solution across the membrane.

5           The balloon 59 can also be positioned adjacent expansion ports 60A coupled with an expansion lumen 60B and drug delivery ports 58 as illustrated in Figure 6D. Different drug solutions can be delivered through the expansion  
10           ports 60B and the drug delivery ports 58. Further, a media suitable for expanding the balloon 59 can be delivered through the expansion lumen 60B and the expansion ports 60A while the drug solution can be delivered through the drug delivery ports 58. When the balloon 59 is constructed from a  
15           membrane or a selectively permeable membrane, a medium which wets the membrane and enhances the permeability of the membrane can be delivered through the expansion ports 60A. A drug solution can be delivered through the drug delivery ports 58 concurrently with or after the wetting medium has been delivered.

15           The ultrasound energy can be generated at an ultrasound energy source which is remote from the ultrasound elements 40 and transmitted via wire to the ultrasound elements 40. Ultrasound can also be internally generated from electrical power delivered to the ultrasound elements 40 from an electrical energy source. A suitable example of an ultrasound element 40 for internal  
20           generation of ultrasound energy includes, but is not limited to, piezoelectric ceramic oscillators. The ultrasound elements 40 can be shaped as a cylinder, a hollow cylinder and a disk which are concentric with the elongated body 34. The ultrasound elements 40 can also be an array of smaller ultrasound elements 40 or a thin plate positioned within the elongated body 34. Similarly,  
25           a single ultrasound element 40 can be composed of several smaller ultrasound elements 40. Suitable frequencies for the ultrasound element include, but are not limited to from 20 KHz to 2MHz.

30           Each ultrasound element 40 can each be individually powered. When the elongated body 34 includes N ultrasound elements 40, the elongated body 34 must include 2N wires to individually power N ultrasound elements 40. The individual ultrasound elements 40 can also be electrically coupled in serial or in parallel as illustrated in Figures 7A and 7B. These arrangements permit

maximum flexibility as they require only  $2N$  wires. Each of the ultrasound elements 40 receive power simultaneously whether the ultrasound elements 40 are in series or in parallel. When the ultrasound elements 40 are in series, less current is required to produce the same power from each ultrasound element 40 than when the ultrasound elements 40 are connected in parallel. The reduced current allows smaller wires to be used to provide power to the ultrasound elements 40 and accordingly increases the flexibility of the elongated body 34. When the ultrasound elements 40 are connected in parallel, an ultrasound element 40 can break down and the remaining ultrasound elements 40 will continue to operate.

As illustrated in Figure 7C, a common wire 61 can provide power to each of ultrasound element 40 while each ultrasound element 40 has its own return wire 62. A particular ultrasound element 40 can be individually activated by closing a switch 64 to complete a circuit between the common wire 61 and the particular ultrasound element's return wire 62. Once a switch 64 corresponding to a particular ultrasound element 40 has been closed, the amount of power supplied to the ultrasound element 40 can be adjusted with the corresponding potentiometer 66. Accordingly, an elongated body 34 with  $N$  ultrasound elements 40 requires only  $N+1$  wires and still permits independent control of the ultrasound elements 40. This reduced number of wires increases the flexibility of the elongated body 34. To improve the flexibility of the elongated body 34, the individual return wires 62 can have diameters which are smaller than the common wire 61 diameter. For instance, in an embodiment where  $N$  ultrasound elements 40 will be powered simultaneously, the diameter of the individual return wires 62 can be the square root of  $N$  times smaller than the diameter of the common wire 61.

As illustrated in Figure 1, the system 10 can include at least one temperature sensor 20. Suitable temperature sensors 20 include, but are not limited to, thermistors, thermocouples, resistance temperature detectors (RTD)s, and fiber optic temperature sensors which use thermalchromic liquid crystals. Suitable temperature sensor 20 geometries include, but are not limited to, a point, patch, stripe and a band around the sheath 12. The

temperature sensors 20 can be positioned on the sheath 12 or on the elongated body 34 near the ultrasound elements 40. The temperature sensors 20 should be positioned so they are exposed to the portion of a treatment section which is receiving drug solution and/or ultrasound energy.

5           The temperature sensors 20 can be electrically connected as illustrated in Figure 8. Each temperature sensor 20 can be coupled with a common wire 61 and then include its own return wire 62. Accordingly,  $N+1$  wires can be used to independently sense the temperature at the temperature sensors 20 when  $N$  temperature sensors 20 are employed. A suitable common wire 61  
10       can be constructed from Constantan and suitable return wires 62 can be constructed from copper. The temperature at a particular temperature sensor 20 can be determined by closing a switch 64 to complete a circuit between the thermocouple's return wire 62 and the common wire 61. When the  
15       temperature sensors 20 are thermocouples, the temperature can be calculated from the voltage in the circuit. To improve the flexibility of the sheath 12, the individual return wires 62 can have diameters which are smaller than the common wire 61 diameter.

Each temperature sensor 20 can also be independently wired. Employing  $N$  independently wired temperature sensors 20 requires  $2N$  wires to  
20       pass the length of the sheath 12.

The sheath 12 or elongated body 34 flexibility can also be improved by using fiber optic based temperature sensors 20. The flexibility can be improved because only  $N$  fiber optics need to be employed sense the temperature at  $N$  temperature sensors 20.

25           The system 10 can include a feedback control system 68 as illustrated in Figure 9. The temperature at each temperature sensor 20 is monitored and the output power of energy source adjusted accordingly. The physician can, if desired, override the closed or open loop system.

30           The feedback control system 68 includes an energy source 70, power circuits 72 and a power calculation device 74 coupled with the ultrasound elements 40. A temperature measurement device 76 is coupled with the temperature sensors 20 on the sheath 12. A processing unit 78 is coupled with

the power calculation device 74, the power circuits 72 and a user interface and display 80.

5 In operation, the temperature at each temperature sensor 20 is determined at the temperature measurement device 76. The processing unit 78 receives each determined temperature from the temperature measurement device 76. The determined temperature can then be displayed to the user at the user interface and display 80.

10 The processing unit 78 includes logic for generating a temperature control signal. The temperature control signal is proportional to the difference between the measured temperature and a desired temperature. The desired temperature can be determined by the user. The user can set the predetermined temperature at the user interface and display 80.

15 The temperature control signal is received by the power circuits 72. The power circuits 72 adjust the power level of the energy supplied to the ultrasound elements 40 from the energy source 70. For instance, when the temperature control signal is above a particular level, the power supplied to a particular ultrasound element 40 is reduced in proportion to the magnitude of the temperature control signal. Similarly, when the temperature control signal is below a particular level, the power supplied to a particular ultrasound element 40 is increased in proportion to the magnitude of the temperature control signal. After each power adjustment, the processing unit 78 monitors the temperature sensors 20 and produces another temperature control signal which is received by the power circuits 72.

20 The processing unit 78 can also include safety control logic. The safety control logic detects when the temperature at a temperature sensor 20 has exceeded a safety threshold. The processing unit 78 can then provide a temperature control signal which causes the power circuits 72 to stop the delivery of energy from the energy source 70 to the ultrasound elements 40.

25 Since, the ultrasound elements 40 may be mobile relative to the temperature sensors 20, it can be unclear which ultrasound transducer should have a power level adjustment. As a result, the power level may be identically adjusted at each ultrasound element 40. Further, the power supplied to each of

the ultrasound elements 40 may be adjusted in response to the temperature sensor 20 which indicates the highest temperature. Making power adjustments in response to the temperature of the temperature sensor 20 indicating the highest temperature can prevent overheating of the treatment site.

5           The processing unit 78 also receives a power signal from a power calculation device 74. The power signal can be used to determine the power being received by each ultrasound element 40. The determined power can then be displayed to the user on the user interface and display 80.

10           The feedback control system 68 can maintain the tissue adjacent to the ultrasound elements 40 at a desired temperature for a selected period of time. As described above, the ultrasound elements 40 can be electrically connected so each ultrasound element 40 can generate an independent output. The output maintains a selected energy at each ultrasound element 40 for a selected length of time.

15           The processing unit 78 can be a digital or analog controller, or a computer with software. When the processing unit 78 is a computer it can include a CPU coupled through a system bus. The user interface and display 80 can be a mouse, keyboard, a disk drive, or other non-volatile memory systems, a display monitor, and other peripherals, as are known in the art.

20           Also coupled to the bus is a program memory and a data memory.

          In lieu of the series of power adjustments described above, a profile of the power delivered to each ultrasound element 40 can be incorporated in the processing unit 78 and a preset amount of energy to be delivered may also be profiled. The power delivered to each ultrasound element 40 can be

25           adjusted according to the profiles.

          Figures 10A-10G illustrate a method for using the system 10. In Figure 10A, a guidewire 84 similar to a to a guidewire used in typical angioplasty procedures is directed through vessels 86 toward a treatment site 88 which includes a clot 90. The guidewire 84 is directed through the clot 90.

30           Suitable vessels include, but are not limited to, cardiovascular vessels, the pancreas, sinuses, esophagus, rectum, gastrointestinal vessels and urological vessels.

In Figure 10B, the utility lumen 28 of the sheath 12 is slid over the guidewire 84 and the sheath 12 is advanced along the guidewire 84 using traditional over-the-guidewire techniques. The sheath 12 is advanced until the energy delivery section 18 of the sheath 12 is positioned at the clot 90. Radio opaque markers may be positioned at the energy delivery section 18 of the sheath 12 to aid in the positioning of the sheath 12 within the treatment site 88.

In Figure 10C, the guidewire 84 is withdrawn from the utility lumen 28 by pulling the guidewire 84 proximally while holding the sheath 12 stationary. In Figure 10D, a temperature monitor 92 is coupled with the temperature sensor leads 24, a cooling fluid source 94 is coupled with the cooling fluid inlet and a drug solution source 96 is coupled with the drug inlet port 32. The drug solution source 96 can be a syringe with a Luer fitting which is complementary with the drug inlet port 32. Pressure can be applied to a plunger 98 on the drug solution source 96 to drive the drug solution through the drug delivery lumen 56. The drug solution is delivered from the drug delivery lumen 56 through the drug delivery ports 58 as illustrated by the arrows 100 in Figure 10E. Suitable drug solutions include, but are not limited to, an aqueous solution containing Heparin, Urokinase, Streptokinase, or tissue Plasminogen Activator (TPA).

In Figure 10F, the elongated body 34 is inserted into the utility lumen 28 until the ultrasound element 40 is positioned within the energy delivery section 18. To aid in placement of the ultrasound element 40 within the energy delivery section 18, radiopaque markers may be positioned on the elongated body 34 adjacent to each of the ultrasound elements 40. The ultrasound elements 40 themselves can be radiopaque. Once the elongated body 34 is properly positioned, the ultrasound element 40 is activated to deliver ultrasound energy through the energy delivery section 18 to the clot 90. Suitable ultrasound energy is delivered with a frequency from 20 KHz to 2MHz. While the ultrasound energy is being delivered, the ultrasound element 40 can be moved within the energy delivery section 18 as illustrated by the arrows 52. The movement of the ultrasound element 40 within the energy delivery section 18 can be caused by manipulating the body proximal section

while holding the sheath proximal section stationary. A cooling fluid is flowed through the cooling fluid lumen 44 and out the occlusion device 22.

The cooling fluid can be delivered before, after, during or intermittently with the delivery of the ultrasound energy. Similarly, the drug solution can be delivered before, after, during or intermittently to the delivery of ultrasound energy. As a result, the acts illustrated in Figures 10A-10F can be performed in different orders than are described above. The drug solution and energy are applied until the clot 90 is partially or entirely dissolved as illustrated in Figure 10G. Once the clot 90 has been dissolved to the desired degree, the sheath 12 and elongated body 34 are withdrawn from the treatment site 88.

Figures 11A-11B illustrate a method for using the system 10 when the sheath distal end 16 includes a balloon 59. The sheath 12 is advanced through a vessel 86, as described above, until the balloon 59 is positioned adjacent a clot 90 as illustrated in Figure 11A. The balloon 59 is expanded until the balloon 59 contacts the clot 90 as illustrated in Figure 11B. As described above, the balloon 59 can be expanded by delivering a drug solution through an expansion port 60A or a drug delivery port 58 or by delivering an expansion media through an expansion port 60A. Once the balloon 59 contacts the clot 90, the drug solution or components of the drug solution are driven across the membrane so the drug solution or the components of the drug solution contact the clot 90. The elongated body 34 can be inserted into the sheath 12 before, after or concurrently with the expansion of the balloon 59 and/or the delivery of the drug solution. Similarly, the ultrasound element 40 can be operated before, after, intermittently or concurrently with the expansion of the balloon 59 and/or the delivery of the drug solution.

The foregoing description of a preferred embodiment of the invention has been presented for purposes of illustration and description. It is not intended to be exhaustive or to limit the invention to the precise forms disclosed. Obviously, many modifications, combinations and variations will be apparent to practitioners skilled in this art.

## CLAIMS

What is claimed is:

- 1        1.        A system for delivering ultrasound energy to a treatment section in a  
2        vessel, comprising:  
3                a sheath having a utility lumen and an energy delivery section at least  
4        partially constructed from a material which transmits ultrasound energy;  
5                a drug delivery member having a plurality of drug delivery ports  
6        which are positioned adjacent the energy delivery section; and  
7                an elongated body including at least one ultrasound element and  
8        configured to be movably positioned within the utility lumen to transmit the  
9        ultrasound energy from the ultrasound element through the energy delivery  
10       section.  
  
1        2.        The system of claim 1, wherein the plurality of drug delivery ports  
2        have geometries which cause a substantially equal flow of a drug solution from  
3        each drug delivery port.  
  
1        3.        The system of claim 2, wherein the drug delivery ports increase in size  
2        in a distal direction along the drug delivery member.  
  
1        4.        The system of claim 2, wherein the drug delivery ports are slit shaped.  
  
1        5.        The system of claim 1, wherein the density of the drug delivery port  
2        increases in a distal direction along the drug delivery member.  
  
1        6.        The system of claim 1, wherein the drug delivery member is integral  
2        with the sheath.  
  
1        7.        The system of claim 1, wherein the drug delivery member is external to  
2        the sheath.

1        8.     The system of claim 1, wherein the drug delivery member is wound  
2        around the energy delivery section.

1        9.     The system of claim 1, further comprising:  
2                at least one second drug delivery member including drug delivery ports  
3        positioned adjacent the energy delivery section.

1        10.    The system of claim 1, wherein the sheath includes a support section  
2        which provides the sheath with support and kink resistance.

1        11.    The system of claim 10 wherein the support section is constructed from  
2        copolyester.

1        12.    The system of claim 1, wherein the energy delivery section is  
2        constructed from polyimide.

1        13.    The system of claim 1, further comprising:  
2                an occluding device positioned at a distal end of the sheath and having  
3        a geometry preventing the ultrasound element from exiting a distal end of the  
4        utility lumen.

1        14.    The system of claim 13, wherein the utility lumen extends through the  
2        occluding device and is configured to receive a guidewire.

1        15.    The system of claim 1, wherein the utility lumen is configured to  
2        receive a guidewire.

1        16.    The system of claim 1, further comprising:  
2                at least one second ultrasound element included in the elongated body.

1        17.    The system of claim 1, wherein positioning the elongated body within  
2        the utility lumen forms a lumen between a side of the utility lumen and a  
3        surface of the elongated body and the lumen is configured to receive an  
4        ultrasound element cooling fluid.

1        18. The system of claim 1, further comprising:  
2                at least one temperature sensor positioned at a sheath distal end.

1        19.    The system of claim 18, further comprising:  
2                a feedback control system for adjusting a power delivered to the  
3        ultrasound element in response to a signal from the at least one temperature  
4        sensor.

1        20.    The system of claim 1, further comprising:  
2                a balloon positioned at the energy delivery section.

1        21.    The system of claim 1, wherein the balloon is constructed from a  
2        membrane.

1        22.    The system of claim 1, wherein the balloon is constructed from a  
2        selectively permeable material.

1        23.    A sheath for delivering ultrasound energy to a treatment section in a  
2        vessel, comprising:  
3                a utility lumen configured to movably receive an elongated body with  
4        an ultrasound element;  
5                an energy delivery section at least partially constructed from a material  
6        which transmits ultrasound energy from the ultrasound element; and  
7                a plurality of drug delivery ports positioned adjacent the energy  
8        delivery section.

- 1        24.    The sheath of claim 23, wherein the plurality of drug delivery ports  
2        have geometries which cause a substantially equal flow of a drug solution from  
3        each drug delivery port.
- 1        25.    The sheath of claim 23, wherein the drug delivery ports increase in size  
2        in a distal direction along the drug delivery member.
- 1        26.    The sheath of claim 25, wherein the drug delivery ports are slit shaped.
- 1        27.    The sheath of claim 23, wherein the density of the drug delivery port  
2        increases in a distal direction along the drug delivery member.
- 1        28.    The sheath of claim 23, further comprising:  
2        a drug delivery member which includes the drug delivery ports.
- 1        29.    The system of claim 28, wherein the drug delivery member is external  
2        to the sheath.
- 1        30.    The sheath of claim 29 wherein the drug delivery member is wound  
2        around the energy delivery section.
- 1        31.    The sheath of claim 23, wherein the sheath includes a support section  
2        which provides the sheath with support and kink resistance.
- 1        32.    The sheath of claim 31 wherein the support section is constructed from  
2        copolyester.
- 1        33.    The sheath of claim 23, wherein the energy delivery section is  
2        constructed from polyimide.
- 1        34.    The sheath of claim 23, further comprising:

1           an occluding device positioned at a distal end of the sheath and having  
2           a geometry configured to prevent the ultrasound element from exiting a distal  
3           end of the utility lumen.

1       35.    The sheath of claim 34, wherein the utility lumen extends through the  
2           occluding device and is configured to receive a guidewire.

1       36.    The sheath of claim 23, wherein the utility lumen is configured to  
2           receive a guidewire.

1       37.    The sheath of claim 23, wherein positioning the elongated body within  
2           the utility lumen forms a lumen between a side of the utility lumen and a  
3           surface of the elongated body and the lumen is configured to receive an  
4           ultrasound element cooling fluid.

1       38.    The sheath of claim 23, further comprising:  
2           at least one temperature sensor positioned at a sheath distal end.

1       39.    The sheath of claim 38, further comprising:  
2           a feedback control system for adjusting a power delivered to the  
3           ultrasound element in response to a signal from the at least one temperature  
4           sensor.

1       40.    A system for delivering ultrasound energy to a treatment section in a  
2           vessel, comprising:  
3           a sheath having a utility lumen configured to movably receive an  
4           elongated body with an ultrasound element and an energy delivery section at  
5           least partially constructed from a material which transmits ultrasound energy  
6           from the ultrasound element; and  
7           a drug delivery member having a plurality of drug delivery ports  
8           which are configured to be positioned adjacent the energy delivery section.

1        41.     The sheath of claim 40, wherein the plurality of drug delivery ports  
2        have geometries which cause a substantially equal flow of a drug solution from  
3        each drug delivery port.

1        42.     The system of claim 40, wherein the density of the drug delivery port  
2        increases in a distal direction along the drug delivery member.

1        43.     The system of claim 40 wherein the drug delivery member is  
2        configured to be wound around the energy delivery section.

1        44.     The system of claim 40, wherein the sheath includes a support section  
2        which provides the sheath with support and kink resistance.

1        45.     The system of claim 44, wherein the support section is constructed  
2        from copolyester.

1        46.     The system of claim 40, wherein the energy delivery section is  
2        constructed from polyimide.

1        47.     The system of claim 40, wherein positioning the elongated body within  
2        the utility lumen forms a lumen between a side of the utility lumen and a  
3        surface of the elongated body and the lumen is configured to receive an  
4        ultrasound element cooling fluid.

1        48.     A sheath for delivering ultrasound energy to a treatment section in a  
2        vessel, comprising:

3                a sheath having a utility lumen configured to movably receive an  
4                elongated body with an ultrasound element and an energy delivery section at  
5                least partially constructed from a material which transmits ultrasound energy  
6                from the ultrasound element; and

7                at least one temperature sensor positioned adjacent the energy delivery  
8        section.

1       49.     The sheath of claim 48, further comprising:  
2             a drug delivery member having a plurality of drug delivery ports  
3       which are configured to be positioned adjacent the energy delivery section.

1       50.     The sheath of claim 49, wherein the plurality of drug delivery ports  
2       have geometries which cause a substantially equal flow of a drug solution from  
3       each drug delivery port.

1       51.     The sheath of claim 48, further comprising:  
2             a feedback control system for adjusting a power delivered to the  
3       ultrasound element in response to a signal from the at least one temperature  
4       sensor.

1       52.     A system for delivering ultrasound energy to a treatment section in a  
2       vessel, comprising:  
3             a sheath having a utility lumen and an energy delivery section at least  
4       partially constructed from a material which transmits ultrasound energy;  
5             an expandable balloon positioned at least partially adjacent the energy  
6       delivery section; and  
7             an elongated body including at least one ultrasound element and  
8       configured to be movably positioned within the utility lumen to transmit the  
9       ultrasound energy from the ultrasound element through the energy delivery  
10      section.

1       53.     The system of claim 52, wherein:  
2       the balloon is constructed from a membrane.

1       54.     The systme of claim 52, wherein:  
2       the balloon is constructed from a selectively permeable membrane.

1        55.    The system of claim 52, further comprising:  
2                a plurality of drug delivery ports included on the sheath within the  
3        balloon.

1        56.    The system of claim 55, wherein the drug delivery ports have  
2        geometries to provide a substantially equal flow of a drug solution from each  
3        drug delivery port.

1        57.    The system of claim 52, wherein the sheath includes a support section  
2        which provides the sheath with support and kink resistance.

1        58.    The system of claim 52, further comprising:  
2                an occluding device positioned at a distal end of the sheath and having  
3        a geometry preventing the ultrasound element from exiting a distal end of the  
4        utility lumen.

1        59.    A system for delivering ultrasound energy to a treatment section in a  
2        vessel, comprising:  
3                a sheath having a utility lumen and an energy delivery section at least  
4        partially constructed from a material which transmits ultrasound energy; and  
5                an elongated body configured to be movably received within the utility  
6        lumen and including a cooling fluid lumen passing sufficiently close to  
7        ultrasound element positioned at a distal end of the elongated body that the  
8        ultrasound element can be cooled by a cooling fluid flowed through the  
9        cooling fluid lumen.

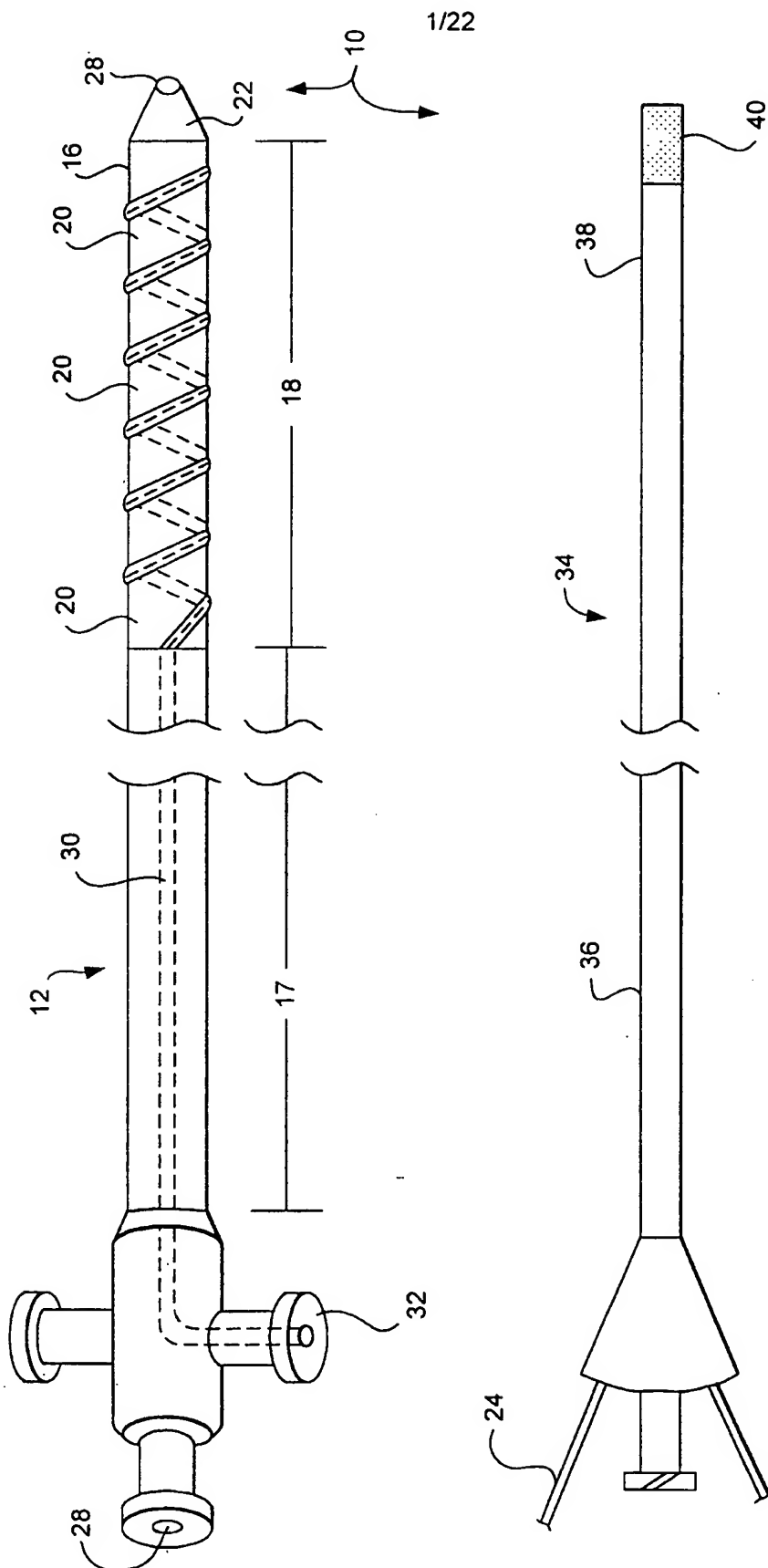


FIG. 1A

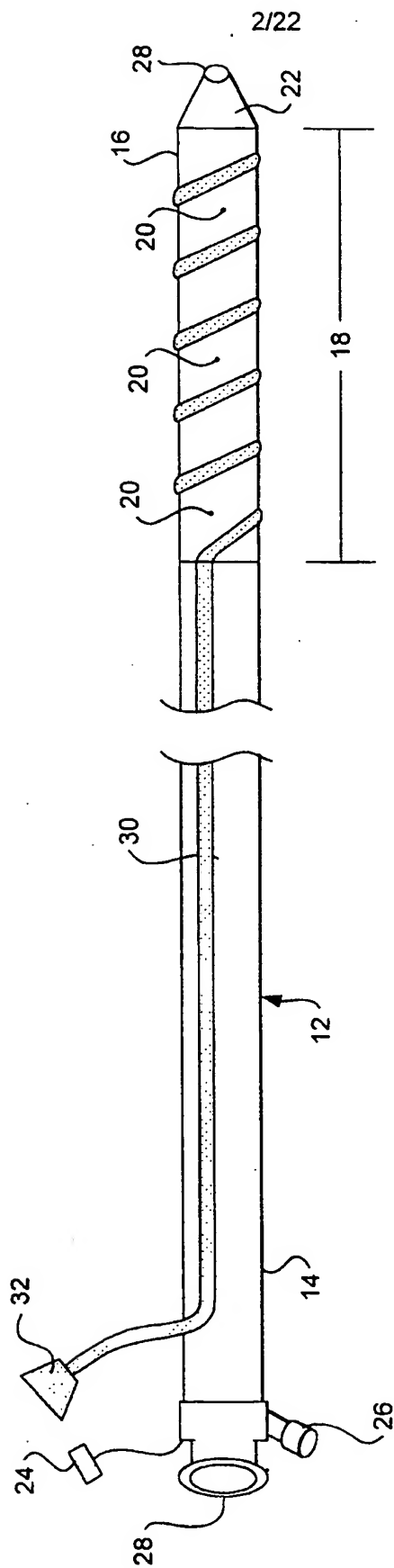


FIG. 1B

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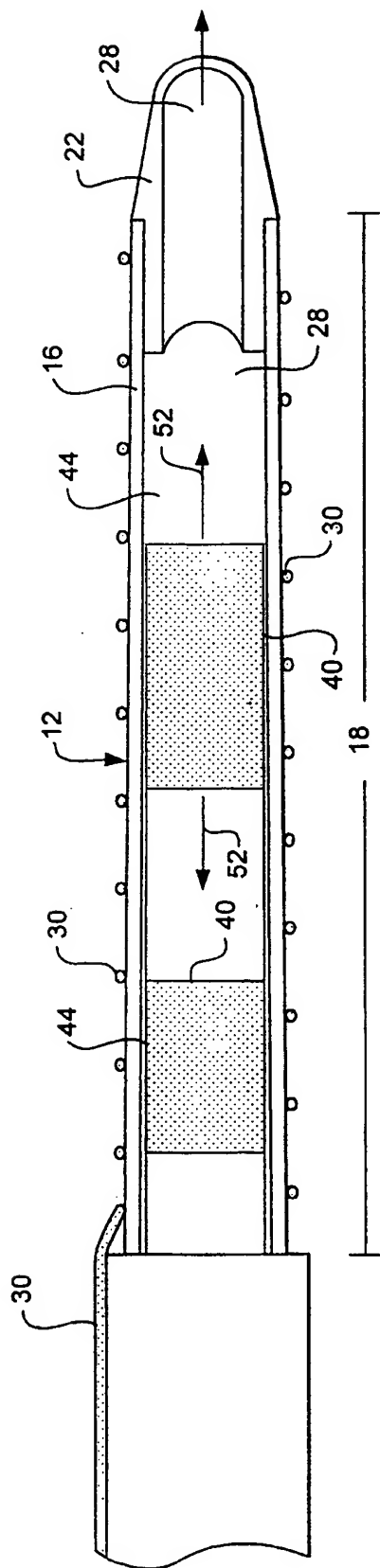


FIG. 2A

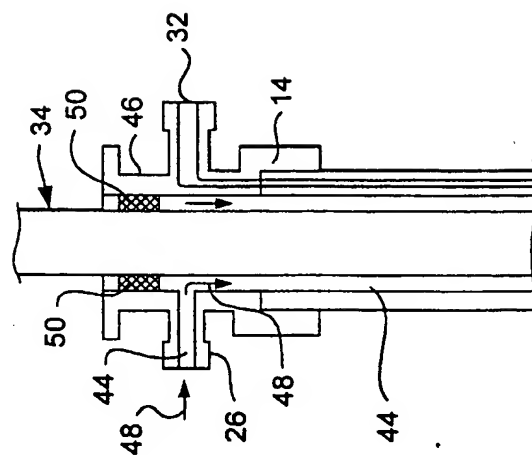
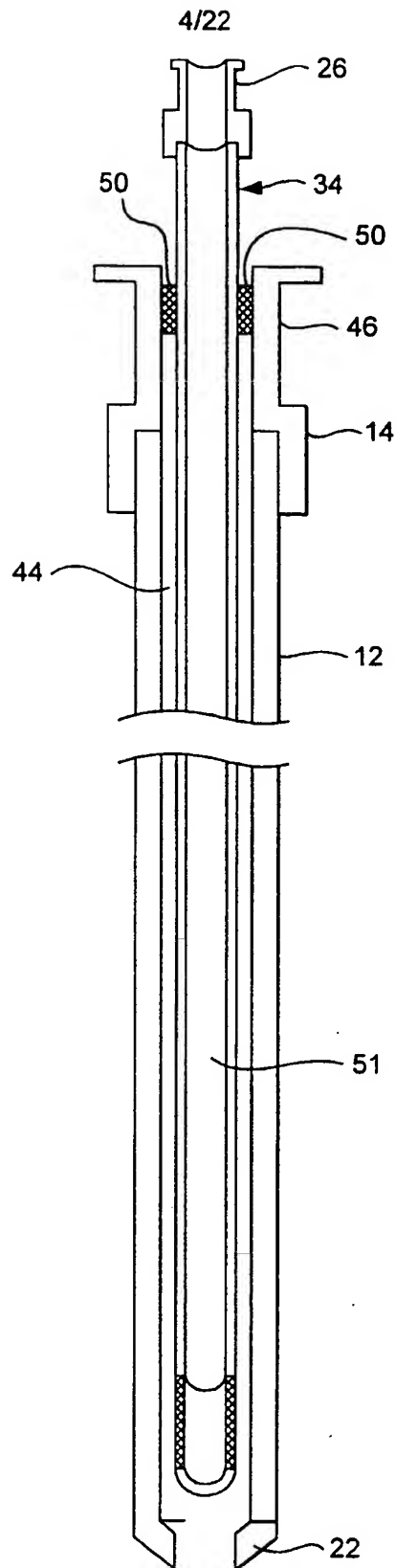


FIG. 2B



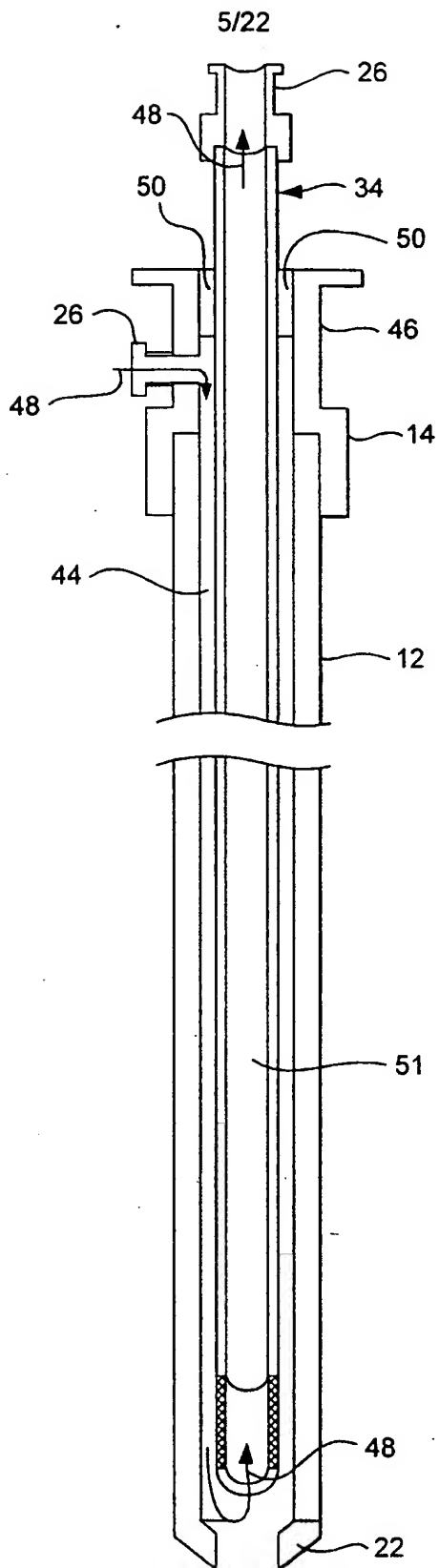
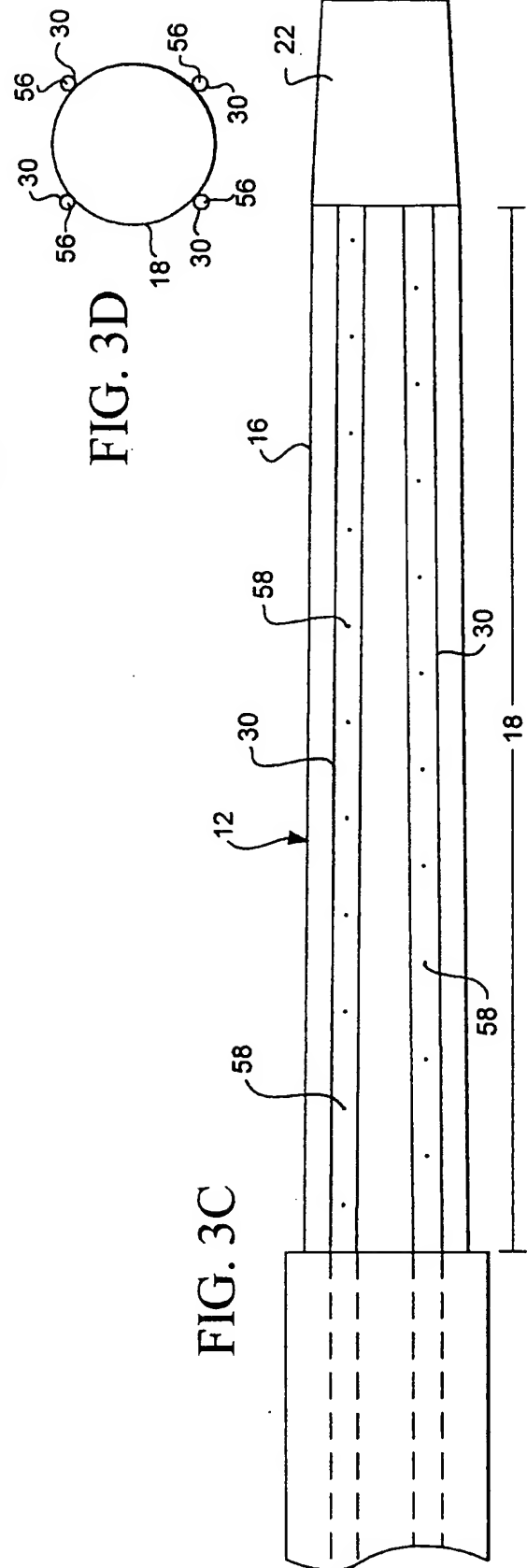
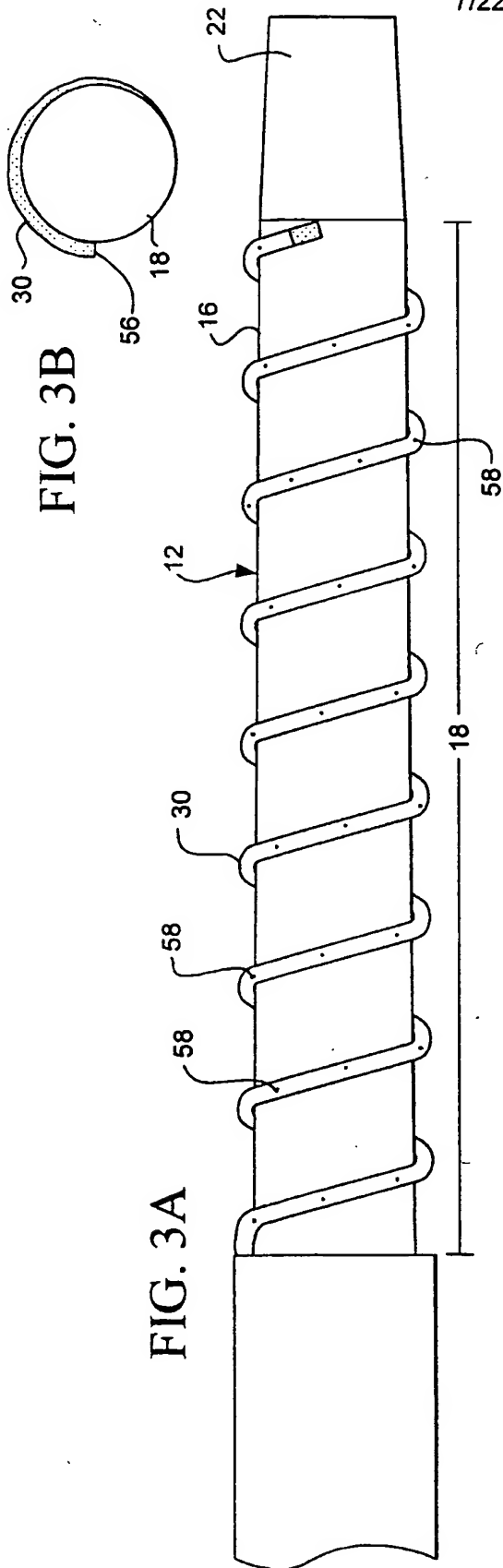


FIG. 2D



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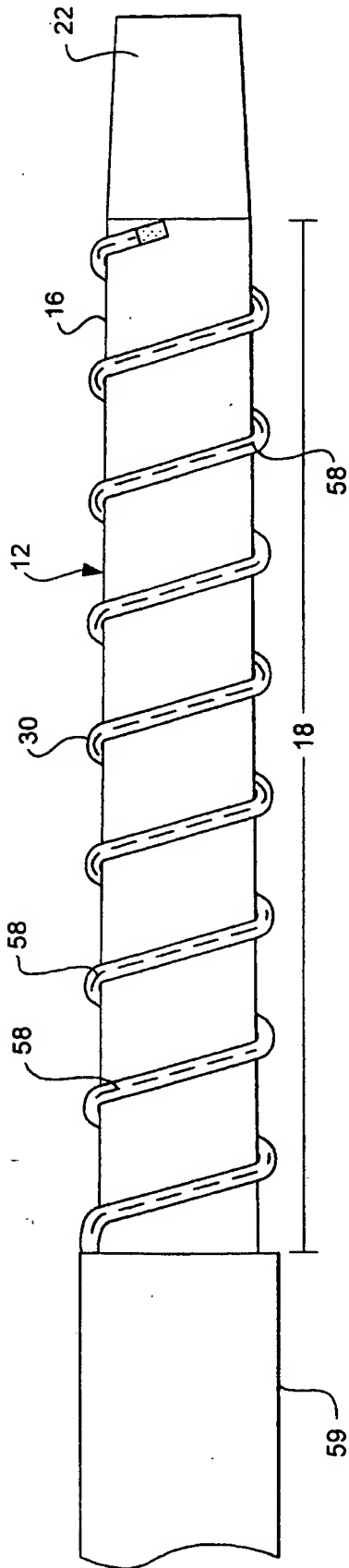


FIG. 3E

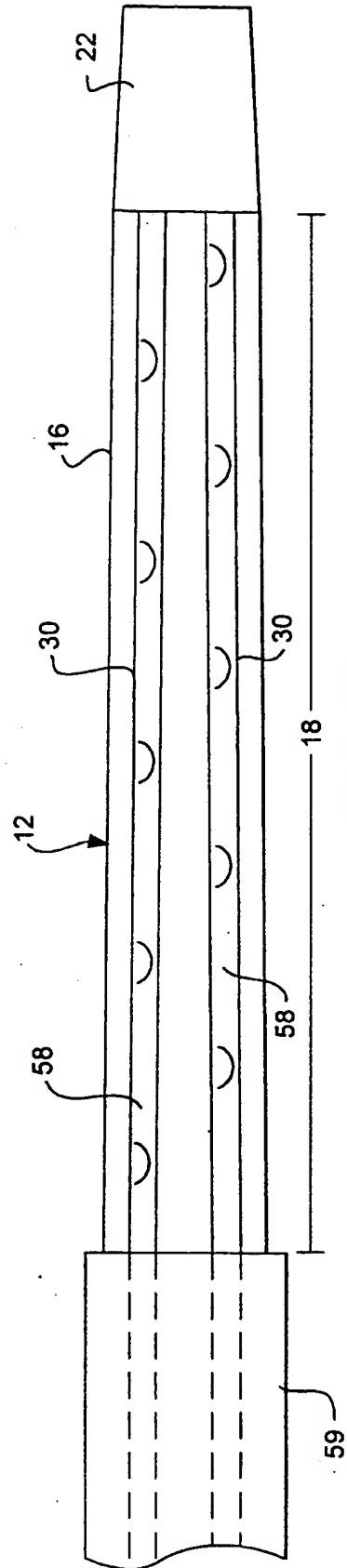


FIG. 3F

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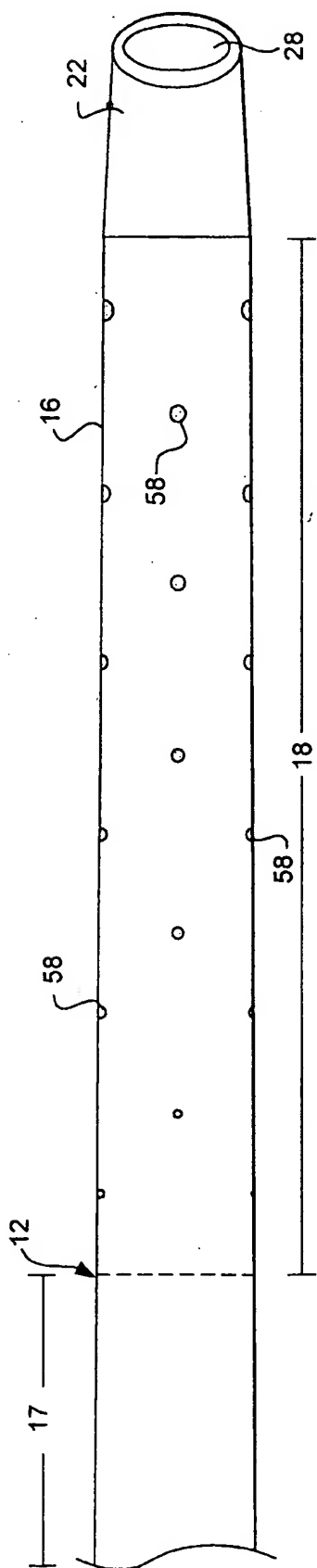


FIG. 4A

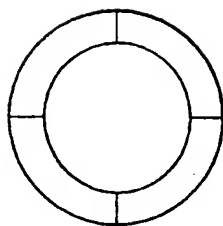


FIG. 4B

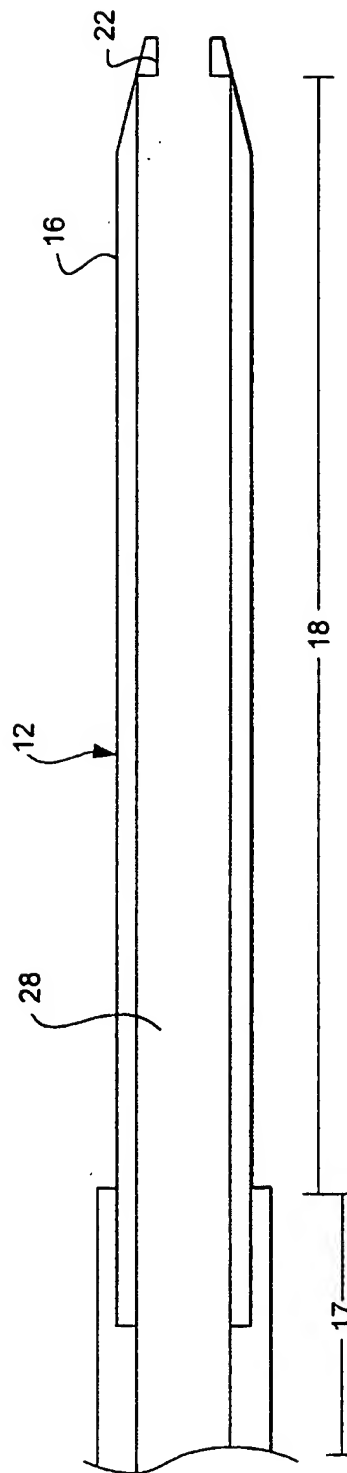


FIG. 5

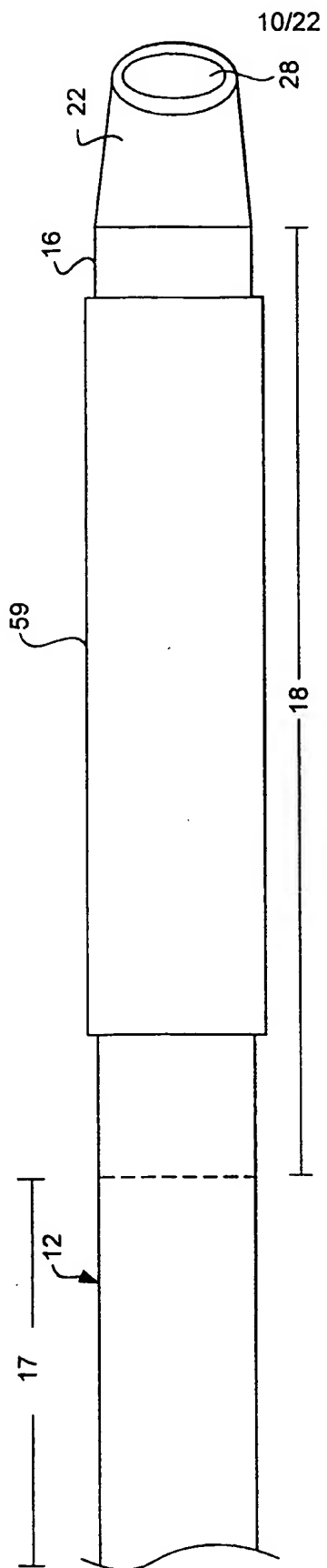


FIG. 6A



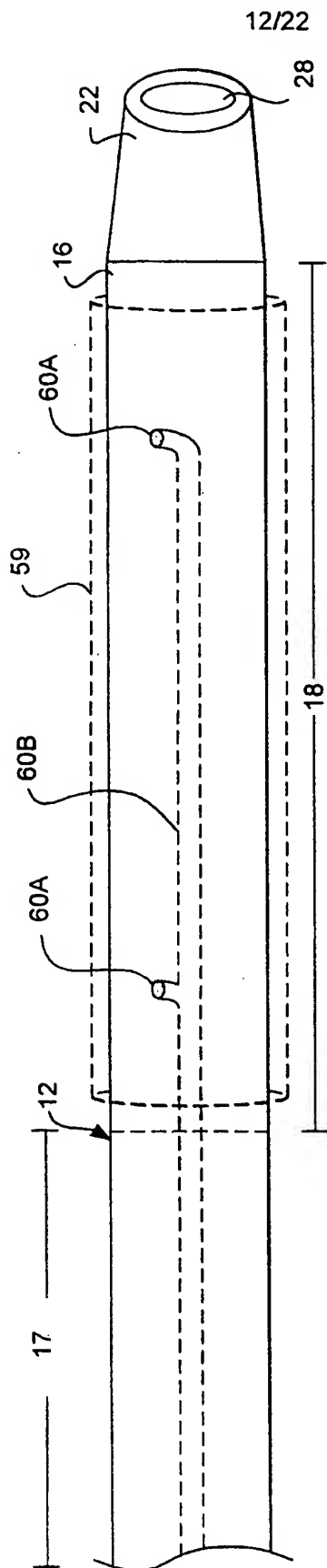


FIG. 6C

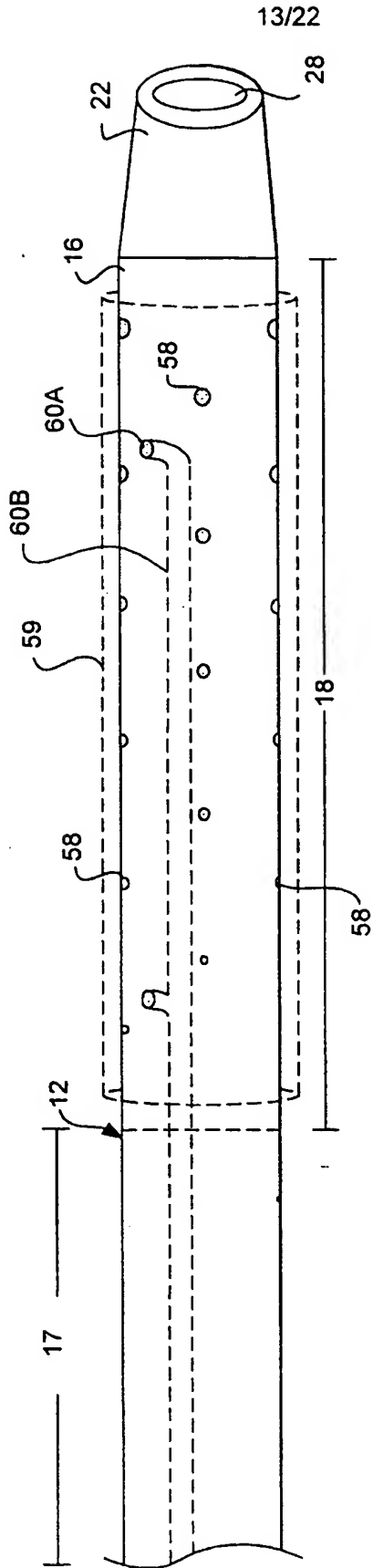


FIG. 6D

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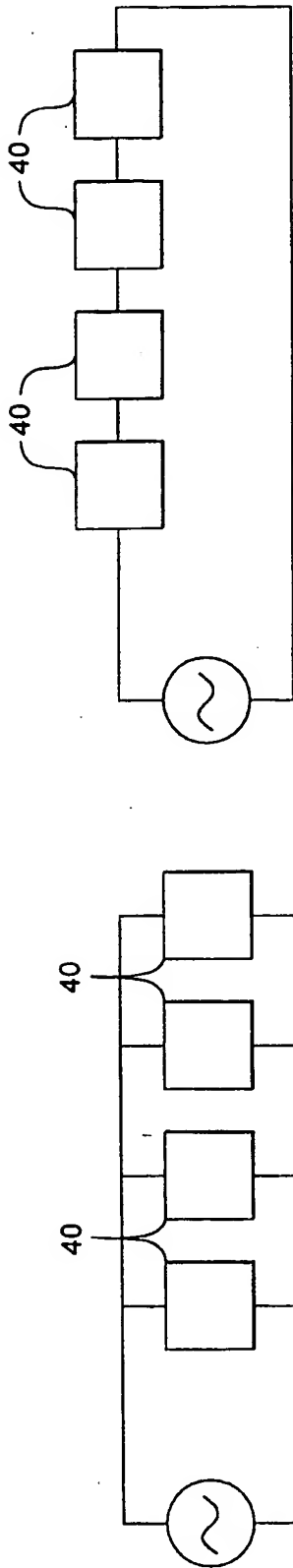


FIG. 7B

FIG. 7A

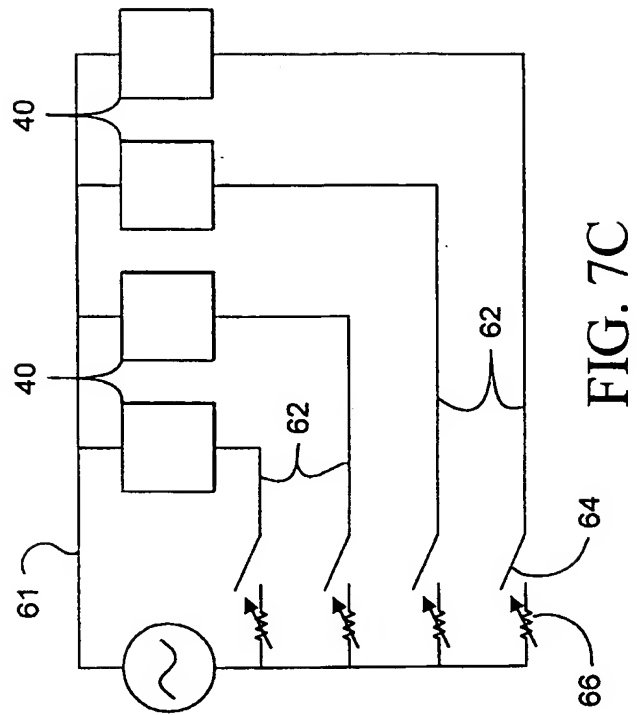


FIG. 7C

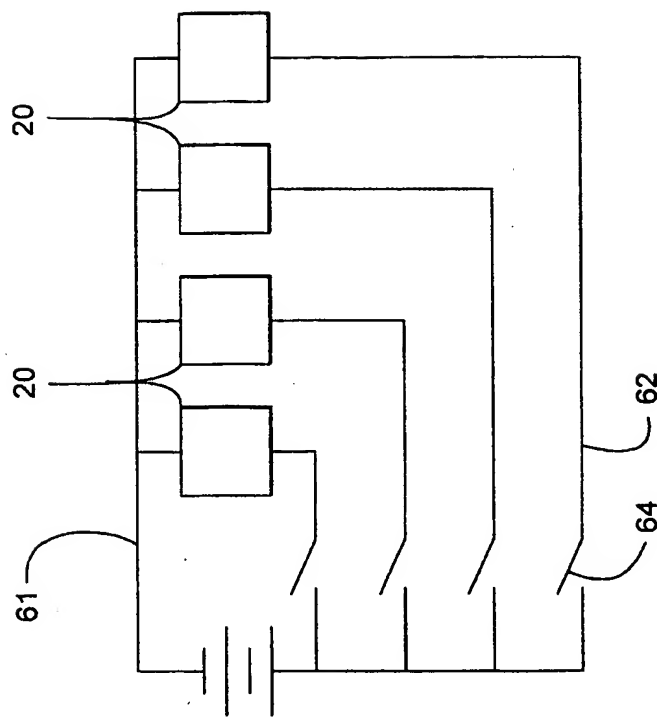


FIG. 8

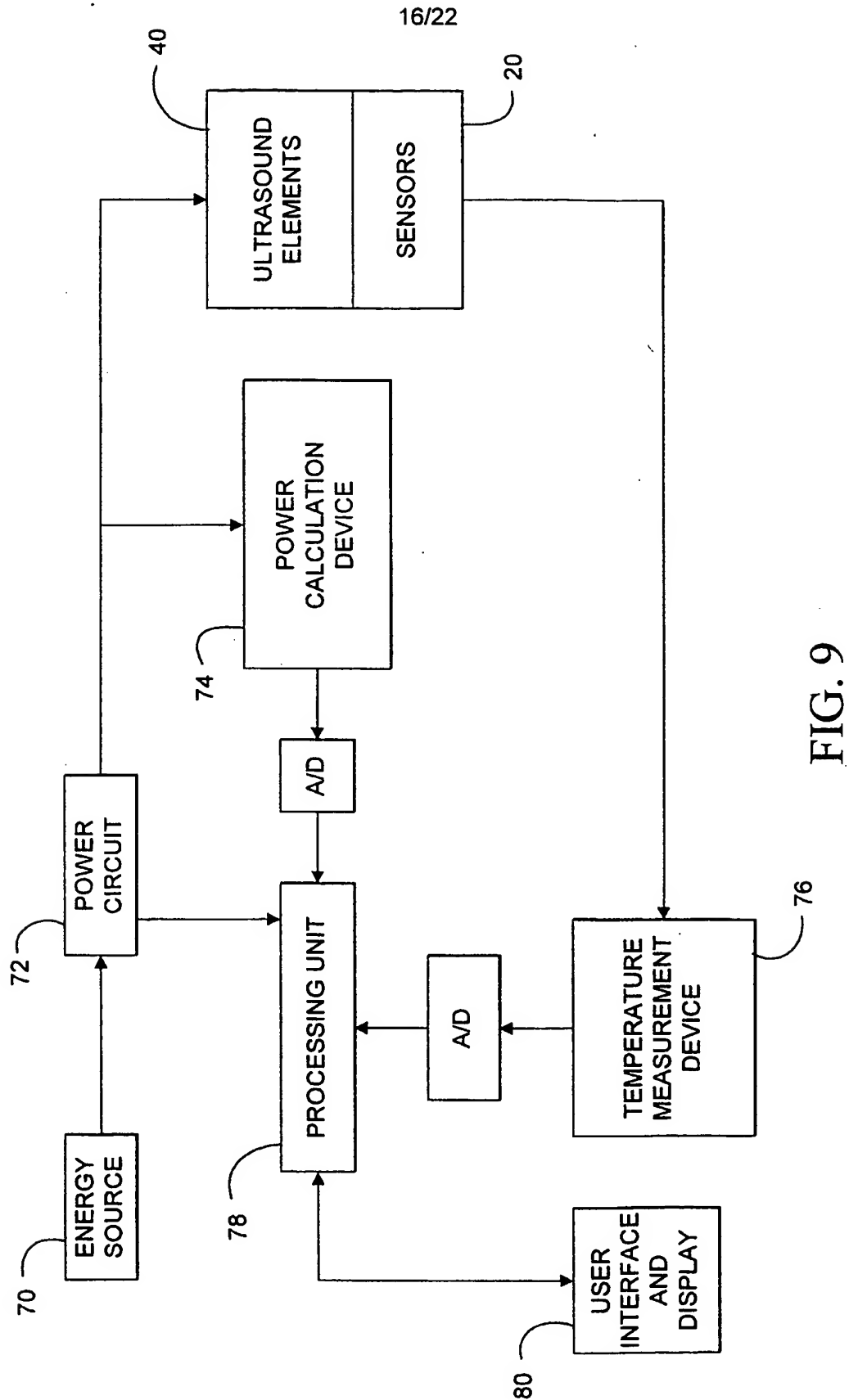


FIG. 9

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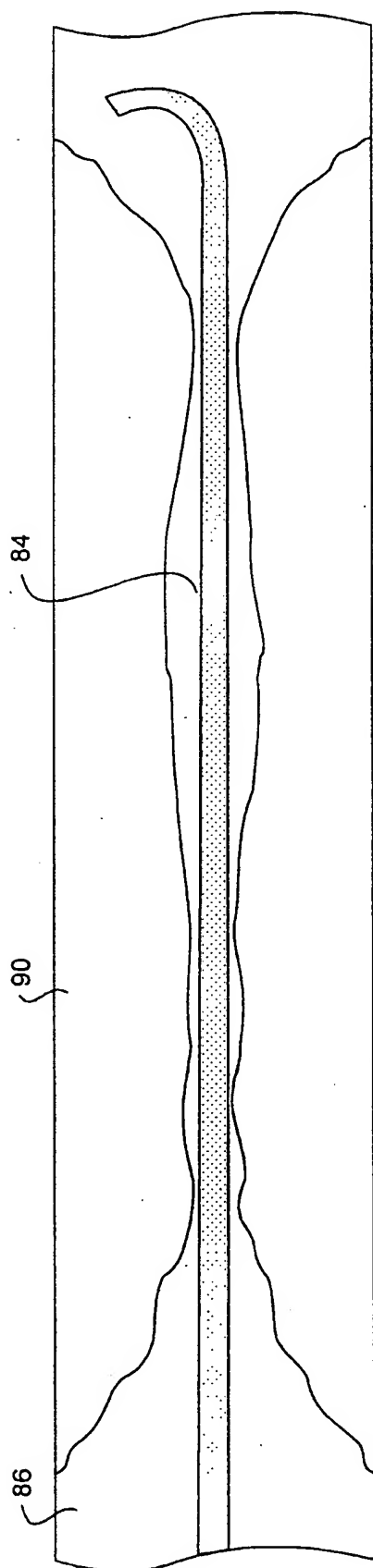


FIG. 10A

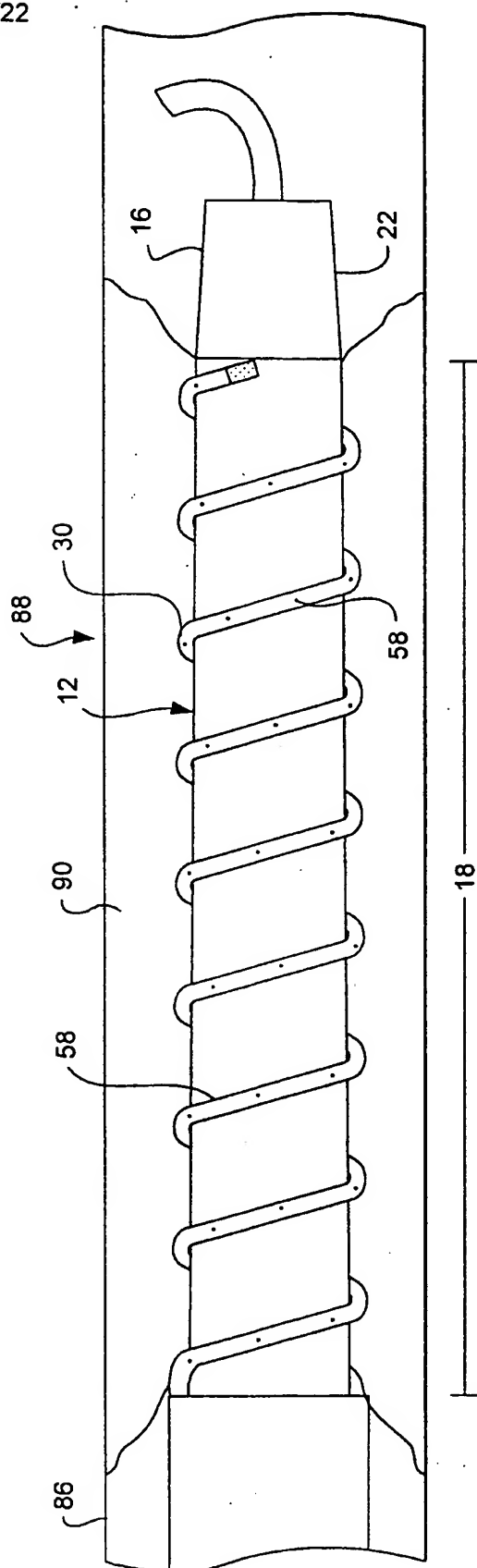
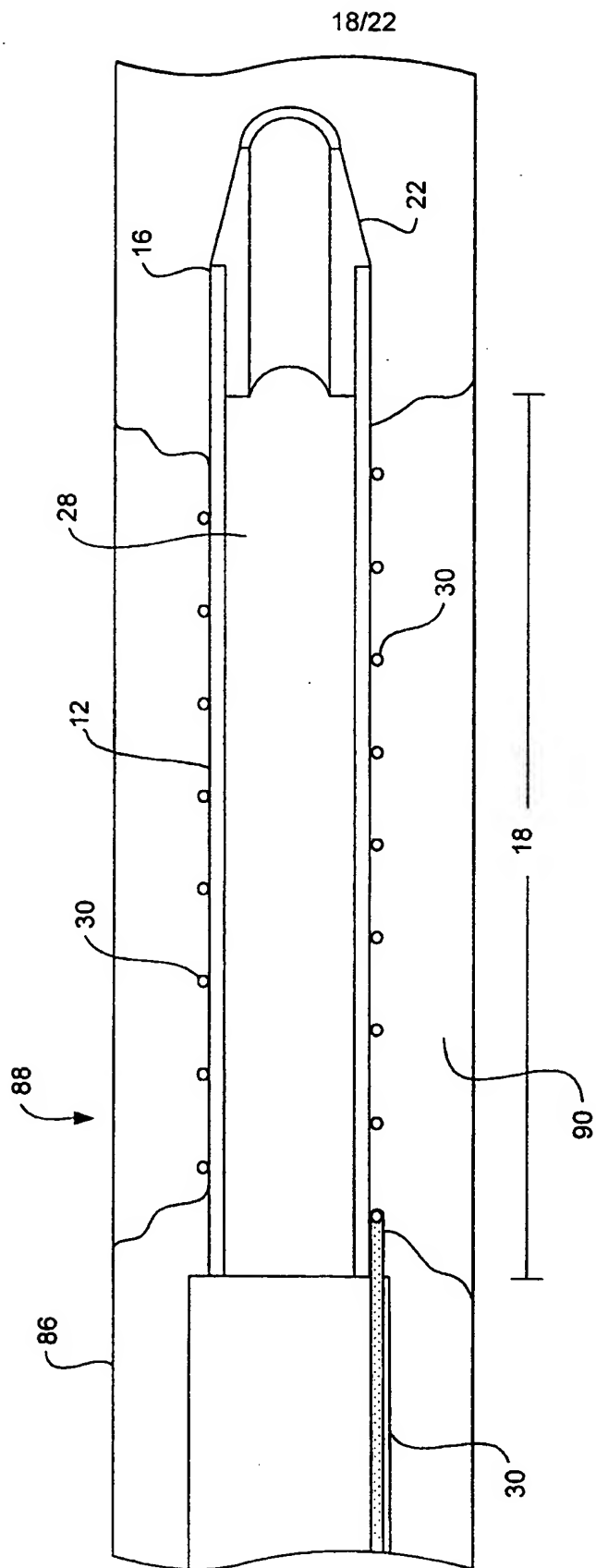


FIG. 10B



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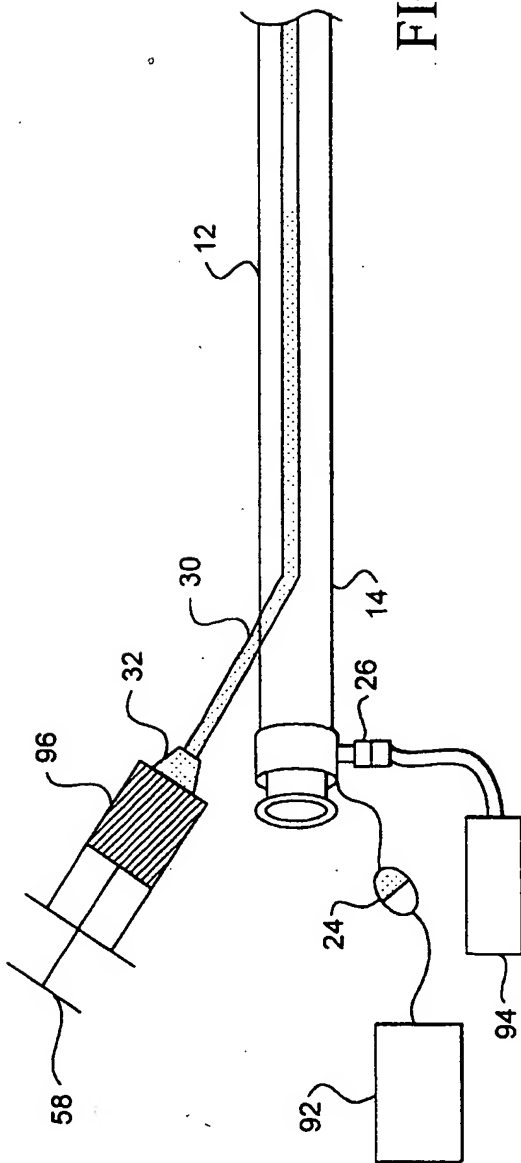


FIG. 10D

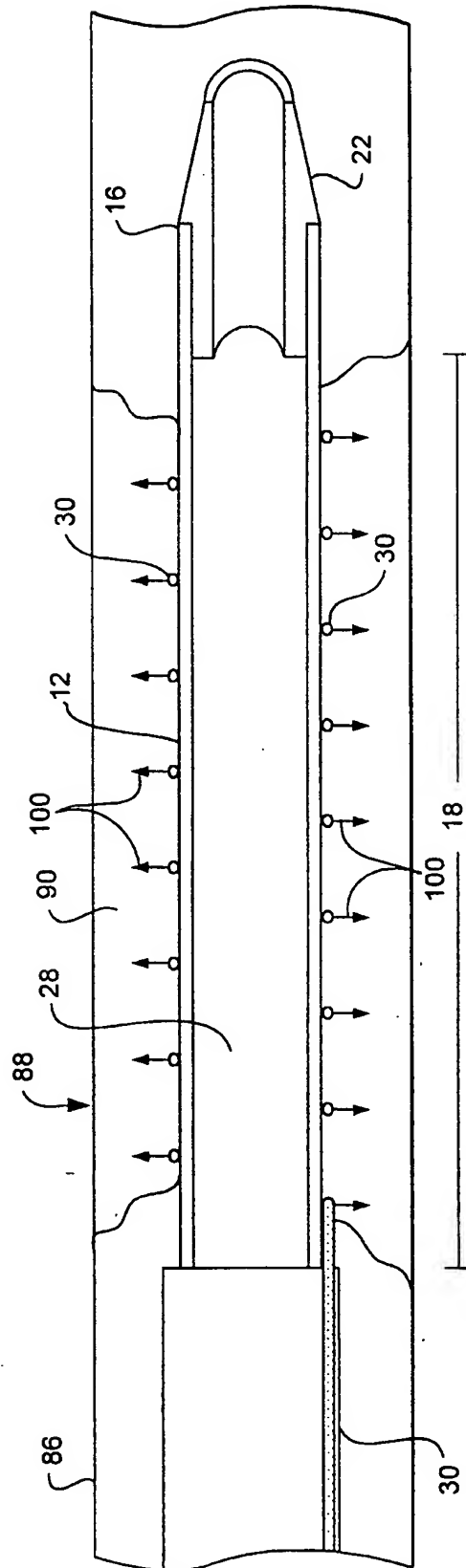


FIG. 10E

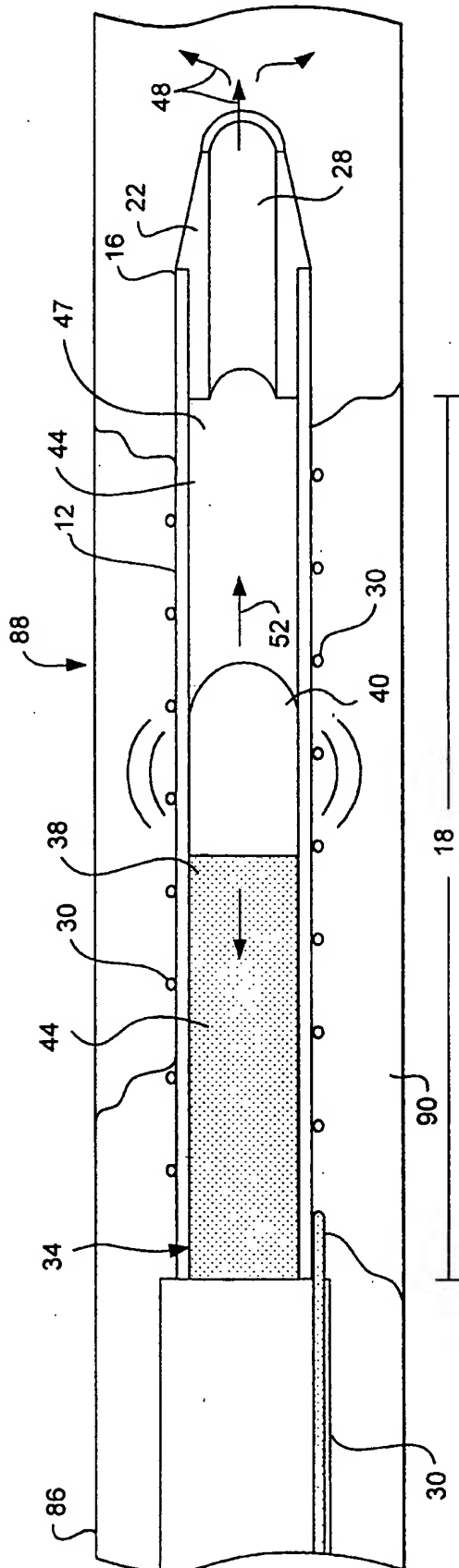


FIG. 10F

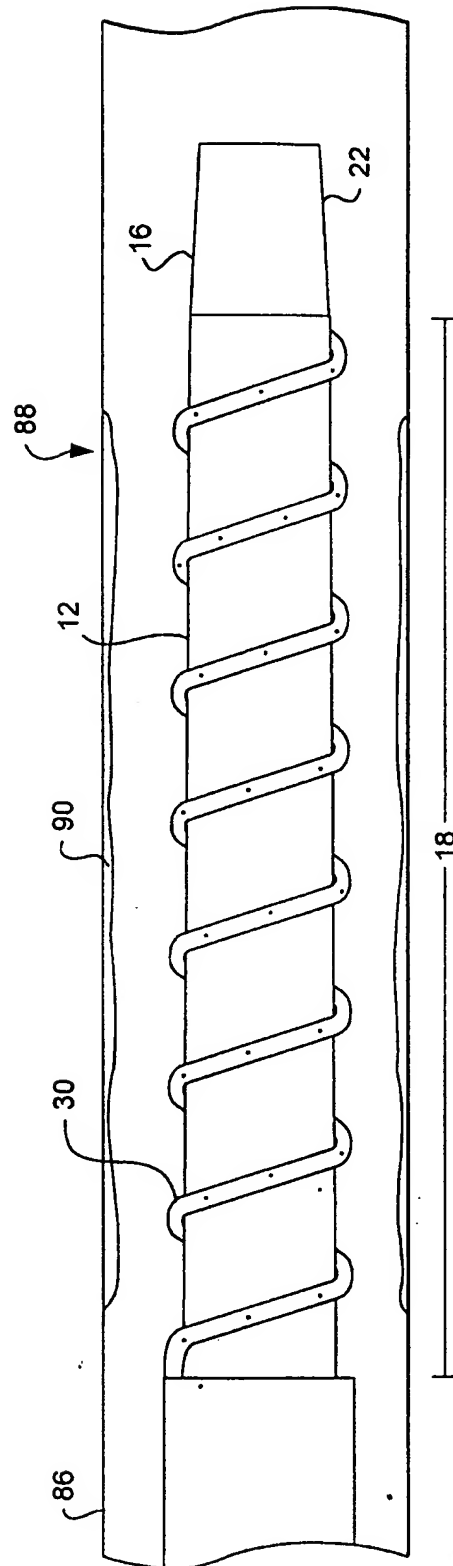
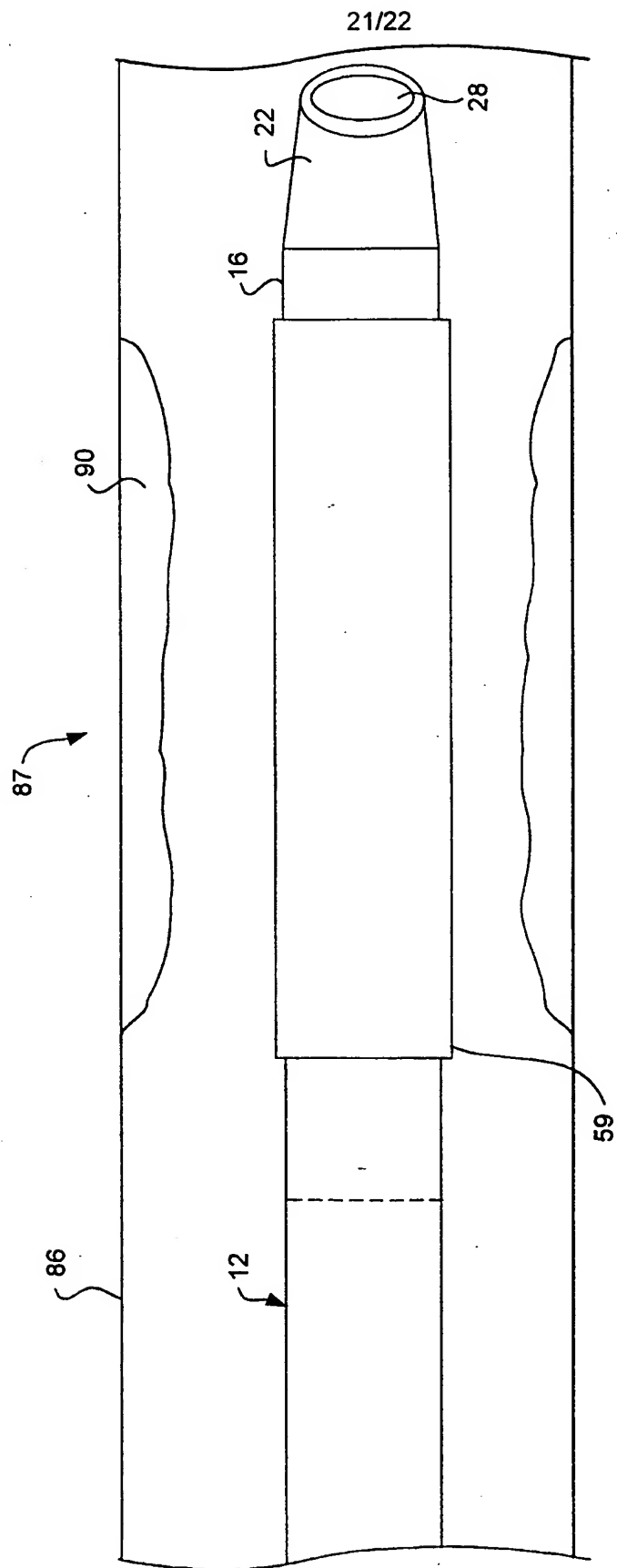


FIG. 10G



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FIG. 11A

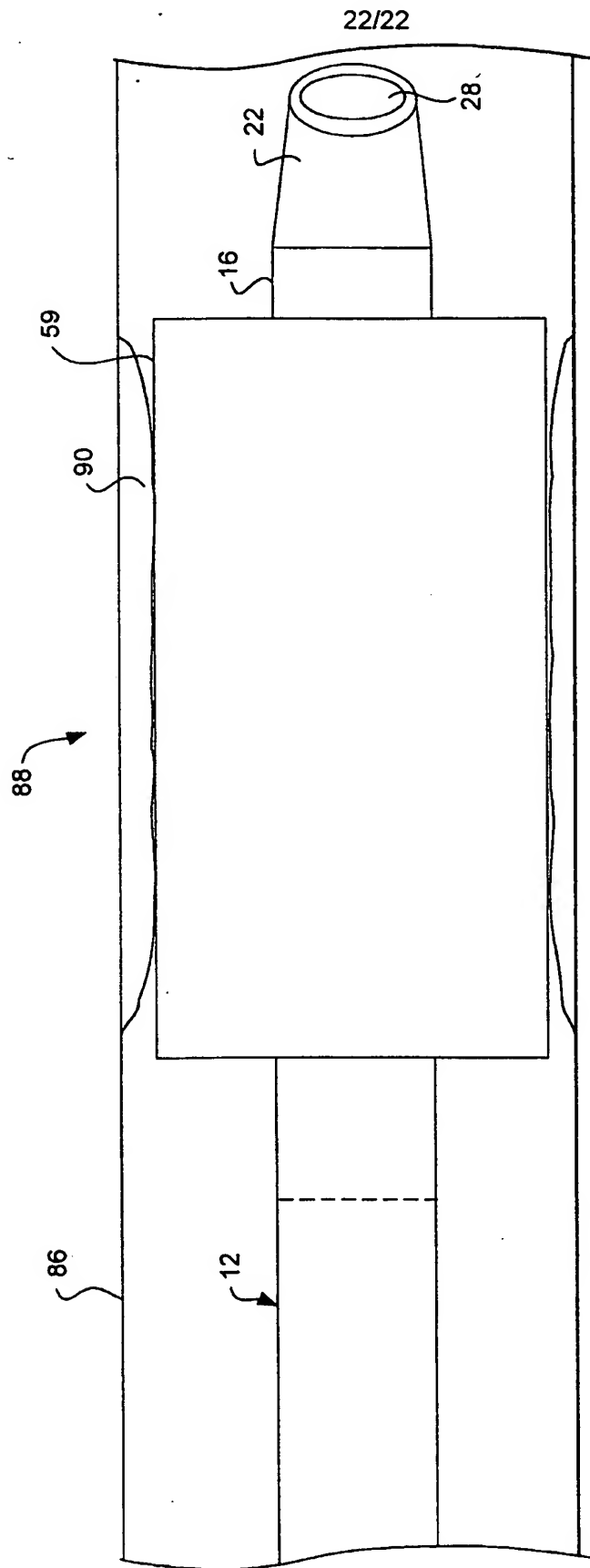


FIG. 11B

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/14757

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61B17/22 A61M37/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61B A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 26777 A (LOCALMED) 12 October 1995 (1995-10-12)	1,23,40
Y	page 11, line 12 - line 15 page 12, line 24 -page 13, line 13; figures 1,2	48-51
X	WO 96 29935 A (BOSTON SCIENT CORP) 3 October 1996 (1996-10-03)	52,53, 57-59
A	page 6, line 12 -page 7, line 6  page 12, line 1 -page 13, line 21; figures 1,2,9-11	1,10,13, 17,20, 23,34, 37,40, 44,47,48
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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Date of the actual completion of the international search

19 October 1999

Date of mailing of the international search report

28/10/1999

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Authorized officer

Moers, R

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/14757

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 05866 A (CORTRAK) 2 March 1995 (1995-03-02) abstract	52-58
A	page 17, line 22 -page 18, line 32 page 21, line 23 -page 22, line 3; figures 6,11	20-22
Y	WO 98 18391 A (EKOS) 7 May 1998 (1998-05-07)	48-51
A	page 13, line 11 -page 17, line 20 page 20, line 22 - line 29 claim 6; figures 4,8,9	1,23,40
A	WO 97 19645 A (PHARMASONICS) 5 June 1997 (1997-06-05) abstract; figures 1,2	1,23,40
A	US 5 656 016 A (OGDEN JOHN E) 12 August 1997 (1997-08-12)	48-51
A	WO 96 04955 A (CORTRAK) 22 February 1996 (1996-02-22) page 24, line 14 - line 21 page 31, line 18 -page 32, line 20; figure 10	1,23,40

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/14757

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1 - 47  
System for delivering ultrasound including a sheath and a drug delivery member including a plurality of ports.
2. Claims: 48 - 51  
System for delivering ultrasound including a sheath and at least one temperature sensor.
3. Claims: 52 - 58  
System for delivering ultrasound including a sheath and an expandable balloon.
4. Claim : 59  
System for delivering ultrasound including a sheath and a cooling fluid lumen.

# INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 99/14757

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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